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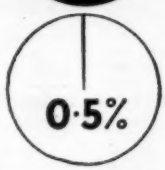

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By H. J. B. Atkins, D.M., M.Ch. Oxfd, F.R.C.S.

ASSISTANT SURGEON TO GUY'S HOSPITAL, LONDON, AND CODIRECTOR OF THE MASTITIS CLINIC

In 1937 a clinic for the investigation and treatment of chronic mastitis was established at Guy's Hospital by Dr. P. M. F. Bishop and myself; we later received valuable help from Mr. P. W. Clarkson. This clinic has been attended by 212 patients with pain or with lumpiness in the breast or with both symptoms. We were at first exercised to define "chronic mastitis," but I have not been able to substitute a better definition than what I suggested in a Hunterian lecture two years ago—namely, "pain or lumpiness of the breast not due to bacterial inflammation, new growth, or fat necrosis" (Atkins 1938). This definition has the one advantage that it frankly proclaims our ignorance of the nature of this disorder, and by adopting it we were able to start our inquiries unimpeded by any preconceived theory.

DEFINITIONS

Early in our investigation it became clear that slight periodic pain in the breast and lumpiness sufficient to distinguish the breast from the surrounding subcutaneous tissue were commonly encountered in patients who never complained of their breasts. We concluded therefore that the presence of these two symptoms did not necessarily imply abnormality. Our definition of chronic mastitis thus tended to be confused until we realised from our microscopical studies that there was no definite distinction between the normal breast and the breast affected with chronic mastitis, the one merging imperceptibly into the other. A definition, therefore, of chronic mastitis which makes such a distinction is undesirable and in fact impossible. In practice we use the term "chronic mastitis" to indicate pain or lumpiness in the breast of sufficient degree to bring the patient to the doctor. This implies that there are women experiencing these two symptoms who, because of fear of cancer or from some other psychological cause, attend the mastitis clinic when their more phlegmatic sisters with breasts similarly affected stay away. Thus a mastitis clinic becomes to some extent the resort of the apprehensive and the mentally unstable, and in assessing the effect of any therapeutic remedy it is especially important to take the psychological element into account.

Throughout this investigation I have borne in mind the possibility of subdividing chronic mastitis into different groups, as was attempted by Cheatle and Cutler (1931). I have not, however, felt justified in differentiating "mazoplasia" from "chronic cystiphorous epithelial hyperplasia" either from our clinical or from our limited histological studies. The distinction drawn by Dawson (1933, 1934) between "epitheliosis" and "adenosis" has been of value in clarifying my idea of the histology of this disease, but I have found that these two changes tend to occur together; hence they do not seem to me to express separate clinical entities. Accordingly we determined to investigate the treatment of the painful nodular breast as a whole, re-examining first the claims of those therapeutic agents which had acquired a reputation for alleviating this disease.

The substances which we investigated were studied from the clinical and, as regards œstrogens and androgens, the histological aspects. In observing the clinical effect of any therapeutic agent, and to eliminate the psychological aspect as far as possible, it was our routine practice in the first place to administer some inert substance, either by mouth or by injection, depending on the method it was intended to adopt subsequently when an active principle was substituted. Thus 31 patients were relieved during the preliminary control period, and these must have consisted largely of those in whom the psychological element predominated and, to a small extent perhaps, of patients in whom the disease underwent a spontaneous cure during the control period. These patients received no further treatment.

EFFECT OF PREGNANCY

While under observation 6 patients became pregnant. In 4 of them all symptoms disappeared between the fifth and sixth months; 1 of these 4 had had mastitis for many years, and a previous pregnancy had caused the symptoms to disappear for about eighteen months; 1 patient was not relieved of her symptoms by the pregnancy; and 1 did not attend the clinic after the tenth week and cannot be traced.

EFFECT OF ŒSTROGENS

We first examined the effect of œstrogens prescribed as œstradiol benzoate given by injection or the synthetic substance stilbœstrol given by mouth. In 1937, when these investigations began, œstrogens were still commonly employed in the treatment of this disease, particularly in America. Patients receiving œstrogens were divided into two groups:

Class 1, receiving less than 80 mg. of œstradiol benzoate by injection in four weeks or 280 mg. of stilbœstrol by mouth in eight weeks.

Class 2, receiving 80 mg. of œstradiol benzoate in four weeks or 280 mg. of stilbœstrol in eight weeks, together with those receiving higher doses or equivalent doses for longer periods.

Class 1 contained 14 patients; these were investigated from the clinical point of view only (table I). In 7 patients there was no change; 4 became worse, and 3 improved. Class 2 contained 19 patients, of whom some were investigated histologically as well as clinically (table II). In 7 of these patients there was no change in the clinical picture; 11 became worse; and in 1 the pain improved but the lumpiness persisted. We concluded therefore that œstrogens were harmful in doses sufficiently large to be effective, and that the larger the dose the more harmful the effect.

Histological effect.—The technique employed in assessing the histological effect of œstrogens was as follows. During the preliminary control period a piece of tissue was removed from the breast under local anæsthesia. This biopsy was performed in an area of the breast where the pain or lumpiness was most evident; if there was a definite lump, a part was removed. A course of œstrogens was then given, and a second biopsy was performed at the end of the course, a piece of breast tissue being taken about ½ in. away from the scar of the first biopsy. In this way it was hoped that the histology of the second piece of tissue removed would not be complicated by the scar from the first operation. This method has the disadvantage that the histological structure of the breast is not uniform, and two areas of breast tissue separated only by ½ in. may have entirely different appearances. Further, since the structure of the breast varies with the menstrual cycle, the second specimen was taken at an interval of four or eight weeks after the first, to ensure that biopsies were performed as far as possible at similar stages in the cycle. The histological effect of a therapeutic agent could be assessed by this method only if the same type of differences between the first and second specimens was found in many cases—13 patients receiving large doses of œstrogen were examined in this way.

The histological features which were specifically studied were: (1) the number of glandular systems in any field (adenosis); (2) the degree of epithelial proliferation within those systems (epitheliosis); and (3) the average size of the lumina of the ducts, the degree of desquamation, and the presence of "pale cells," "pale-celled papillomata," and true papillomata. The fibrous tissue was also examined, and the special points noted were: (1) the degree of differentiation between the periacinous and the subepithelial connective tissue; (2) the fibroblastic activity, as judged by the proportion of active fibroblasts; and (3) the presence or absence of œdema.

In 7 cases no change was found in the degree of adenosis. In 6 cases adenosis was thought to be increased. In 8 cases there was no appreciable difference in epitheliosis between the two sets of sections. In 5 cases epitheliosis was considered to be slightly increased after the administration of œstrogen. There was no characteristic difference either in the average size of the

TABLES I AND II—PATIENTS RECEIVING SMALL AND LARGE DOSES OF ŒSTROGENS

I—SMALL DOSES

Symptoms	No. of cases	Site	No. of cases	Results	No. of cases
(A) Lumpiness and pain	10	BL	6	Both symptoms worse	2
				No effect	4
		UL	4	Both symptoms better	1
				Pain better	1
				Both symptoms worse	1
				No effect	1
(B) Lumpiness only	1	UL	1	No effect	1
(C) Pain only ..	3	BL	1	Worse	1
		UL	2	Improved	1
				No effect	1

II—LARGE DOSES

Symptoms	No. of cases	Site	No. of cases	Results	No. of cases
(A)	9	BL	2	Both symptoms worse	1
				No effect	1
		UL	7	Pain worse, lump same	3
				Pain better, lump same	1
				Both symptoms worse	2
				No effect	1
(B)	1	UL	1	No effect	1
(C)	9	BL	4	Worse	2
				No effect	2
		UL	5	Worse	3
				No effect	2

BL = bilateral; UL = unilateral

lumina of the ducts or in the degree of desquamation between the two sets of specimens. The incidence of "pale cells" and of "pale-celled papillomata" was unaffected in 11 cases. In 1 case both appeared after œstrogen, and in 1 both disappeared. True papillomata were found in 4 instances after injection when they had not been present before. Examination of the fibrous tissue showed no constant change, although there seemed to be a tendency in some cases treated with œstrogens to increased fibroblastic activity, especially of the subepithelial fibrous tissue, which was inclined to be more œdematous than in the control specimens.

In assessing these results we found that the changes were neither sufficiently constant nor sufficiently extensive for us to reach any conclusion from the small series examined. We have received the impression, however, that œstrogens cause an increase in fibroblastic activity, especially of the subepithelial fibrous tissue. Certain of the histological features of chronic mastitis appear therefore to be more advanced after the administration of œstrogens. This tentative assumption corresponds to our clinical findings and, taken in conjunction with them, suggests that abnormal activity of œstrogens may be a factor in the causation of chronic mastitis.

EFFECT OF ANDROGENS

We next investigated the effect of the administration of androgens as testosterone propionate, and patients receiving this substance were again subdivided into two groups:

Class 1, receiving less than 400 mg. of testosterone in four weeks.

Class 2, receiving 400 mg. in four weeks, together with those receiving higher doses or equivalent doses for longer periods.

There were 12 patients in class 1 (table III), and of these 6 improved and 6 showed no change in their clinical condition; 2 patients developed a growth of hair on the upper lip and chin, deepening of the voice, and amenorrhœa. Class 2 contained 22 patients (table IV), of whom 19 improved and 1 became worse; in 2 patients there was no effect; 6 patients developed hirsuties, changes of voice, and amenorrhœa; 1 patient developed cancer of the breast ten months later.

We concluded that patients with chronic mastitis were benefited, so far as the breast condition was concerned, by the doses of testosterone employed, but there was a high proportion of undesirable concomitant effects. Thus, 8 patients developed hirsuties, changes of voice, and amenorrhœa, and menstruation was upset in others. These symptoms persisted in some cases for nine months after the treatment had been stopped.

The age of these patients and the doses of androgens received are set out in table V, which supports the findings of Spence (1939) that it is mostly in younger patients that masculinisation tends to take place. The average age of this group (26) is less than that of all patients receiving androgens; 1 patient aged 40, however, developed these symptoms after relatively small doses of androgens. We have not had an opportunity adequately to follow up our patients treated with androgens, but 4 of those treated with large doses of testosterone propionate and listed as improved have attended my outpatient department since the war with a return of symptoms. Table III shows that, with doses of androgen sufficient to relieve only half the number of patients of their breast symptoms, 2 patients developed hirsuties. Although it seems that in testosterone we have an agent which acts beneficially in these cases, its threshold of effectiveness is so high that it may produce undesirable effects before it can benefit the condition for which it is being given. We therefore believe that the administration of androgens is justifiable at present on experimental grounds alone, and that they should not be prescribed therapeutically until their effects have been studied more carefully.

The case of the patient who developed carcinoma at the site of her lump of mastitis ten months after the administration of testosterone is worth recording in detail in view of the suggestion that this substance might protect patients against cancer of the breast (Loeser 1938). This woman is the only patient of the 212 attending the mastitis clinic who has developed a carcinoma of the breast in the three years since the clinic has been established.

The patient, aged 46, complained of a lump in the left breast for twelve months. This lump completely disappeared for three months and then reappeared five months before she attended the clinic. The lump, which was on the inner side of the breast adjacent to the nipple, bore none of the signs of cancer, and a biopsy from a part of the lump showed typical mastitis.

The patient was given testosterone, 1200 mg. in six weeks, and another biopsy was performed. This section was very

TABLES III AND IV—PATIENTS RECEIVING SMALL AND LARGE DOSES OF ANDROGENS

III—SMALL DOSES

Symptoms	No. of cases	Site	No. of cases	Results	No. of cases
(A) Lumpiness and pain	6	BL	2	Both symptoms improved	2
		UL	4	Both symptoms improved	2
				No effect	2
(B) Lumpiness only	1	BL	1	Diminished in size	1
(C) Pain only ..	5	BL	4	Improved	1
				No effect	3
		UL	1	No effect	1

IV—LARGE DOSES

Symptoms	No. of cases	Site	No. of cases	Results	No. of cases
(A)	17	BL	5	Both symptoms improved	4
				No effect	1
		UL	12	Both symptoms improved	11
				Lumpiness unaffected, pain worse	1
(B)	1	UL	1	Lumpiness became less obvious	1
(C)	4	BL		Improved	3
				No effect	1

similar to the first, except for slightly increased adenosis and decreased fibrous tissue activity. Ten months later the patient came to my outpatient department with a small carcinoma of the breast at the site of the original lump of mastitis. I later performed a radical mastectomy. The cancer was of the spheroidal-celled variety, and the axillary lymph glands were not affected.

Histological effect.—Histological investigation was undertaken in 21 patients receiving large doses of testosterone. The technique employed was the same as that used in the series receiving œstrogens, and the same features were studied in the resulting sections. The

TABLE V—PATIENTS DEVELOPING HIRSUTIES, AMENORRHŒA, AND CHANGES OF VOICE

Case	Age (in years)	Treatment by testosterone propionate	Case	Age (in years)	Treatment by testosterone propionate
1	17	2400 units in 12 weeks	5	26	400 units in 4 weeks
2	19	2200 ,, 8 ,,			4 months' rest
3	19	1200 ,, 12 ,,			400 units in 4 weeks
4	21	400 ,, 8 ,,	6	31	2300 ,, 15 ,,
		6 months' rest	7	36	2400 ,, 12 ,,
		400 units in 8 weeks	8	40	1600 ,, 16 ,,

differences in the histological appearances of the two groups of sections were not so obvious as in the œstrogen series, and even less definite conclusions could therefore be drawn. After the administration of testosterone and with some exceptions (as in the case cited above) there appeared, however, to be a slightly diminished degree of epithelial activity as regards both adenosis and epitheliosis. The subepithelial fibrous tissue tended to decrease in amount and become invaded by the periacinous fibrous tissue. On the whole, although the changes were slight, some of the features of chronic mastitis appeared less advanced in most of the sections taken after the administration of androgens. The limitations of the method employed and the general similarity of the two groups of sections in the testosterone series, together with the small number of cases, made us doubt the value of this part of our investigation into the effect of testosterone on the human breast.

EFFECT OF DIATHERMY

Lastly, a small series of 6 patients was treated with short-wave diathermy (table VI); 1 of these patients did

TABLE VI—PATIENTS RECEIVING DIATHERMY

Symptoms	No. of cases	Site	No. of cases	Results	No. of cases
Lumpiness and pain	3	BL	1	Pain improved	1
		UL	2	Lumpiness and pain improved	1
				Pain improved, lumpiness unaffected	1
Pain only	3	UL	[3	Improved	2
				Untraced	1

not return after the first treatment and could not be traced; the remaining 5 were relieved of their pain at least temporarily; 2 have since returned with recurrence of pain. Some patients not included in this series, because they had previously received œstrogens, were not relieved except for a few hours by diathermy. It is our impression that, as in the case of articular pains, it is those patients who notice that cold damp weather makes the pain worse who are benefited particularly by diathermy.

SUMMARY AND CONCLUSIONS

(1) Chronic mastitis has a large psychological element. In investigating the effect of therapeutic agents it is therefore necessary to exercise the most scrupulous control.

(2) The administration of œstrogens in doses sufficiently large to affect the breast was found to be harmful, and it was thought that the histological changes were advanced by this substance.

(3) Androgens can alleviate the symptoms of most cases of chronic mastitis, but the beneficial effect is not permanent, and undesirable concomitant effects may rob the treatment of its value.

(4) In 1 case of chronic mastitis, the only one of 212 to become malignant, carcinoma of the breast developed ten months after a course of testosterone-propionate injections.

(5) The histological changes in the breast produced by androgens in doses up to the limit of tolerance are insignificant.

(6) Diathermy is of value in alleviating the pain in chronic mastitis, but its effect is liable to be only temporary.

My thanks are due to my colleague and codirector of the mastitis clinic, Dr. Bishop, who has been responsible for the administration of the endocrines and for determining the doses to be used; to Mr. Clarkson, who performed many of the biopsies and helped me to examine the sections; and to Prof. Nicholson, for his advice on histological problems. The expenses of the investigation were defrayed by a grant from the British Empire Cancer Campaign.

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THE NOMENCLATURE OF INFLUENZA

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SINCE the discovery in 1933 (Smith et al.) that a virus pathogenic for ferrets could be recovered from patients with influenza, the same or closely related viruses have been obtained from outbreaks all over the world. The virus is probably the most important cause at the present time of epidemic influenza of man and is generally referred to in the literature as influenza virus or epidemic influenza virus. It has, however, become evident that the clinical picture historically recognised as influenza is not a single ætiological entity; in particular widespread outbreaks have been described (Francis 1937, Stuart-Harris et al. 1940) in which the ferret-pathogenic virus was apparently not concerned. Confusion may thus be introduced by attempting to confine the term "epidemic influenza" to the disease associated with the presence of that virus. It seems wise, therefore, to adopt a more precise terminology. The writers of this note, who are now or were formerly associated with work on influenza at the National Institute for Medical Research or at the laboratories of the International Health Division of the Rockefeller Foundation have agreed to use in future the nomenclature suggested below, and invite the coöperation of other workers in this field of investigation.

SUGGESTED NOMENCLATURE

Clinical influenza.—An ætiologically indefinite symptom-complex long recognised by physicians and characterised by the presence of the clinical manifestations which in recent years have been enumerated and described by Stuart-Harris, Andrewes, and Smith (1938), Francis (1939), Francis, Magill, Beck and Rickard (1937), Horsfall, Hahn and Rickard (1940) and Stuart-Harris, Smith and Andrewes (1940). The term includes the symptom-complexes referred to by Stuart-Harris et al. (1938, 1940) as "febrile catarrhs"; a sharp separation of these on clinical or epidemiological grounds has proved exceedingly difficult to establish.

Influenza A.—A specific disease entity caused by infection with any one of the various strains of the virus discovered by

Smith, Andrewes and Laidlaw (1933) which will hereinafter be termed influenza A virus.

The separation of influenza A leaves a disease or group of diseases clinically resembling it but as yet of unknown ætiology. If and when hitherto undescribed viruses are isolated from this group and are shown to be of ætiological significance other specific diseases in the group could be labelled influenza B, C, &c., as they are found to be caused by the as yet hypothetical agents influenza B virus, C virus, ... &c. ; if agents other than viruses are implicated the diseases in question should be given appropriate names which cannot be confused with those of the virus diseases.

Influenza A virus.—The virus discovered by Smith, Andrewes, and Laidlaw (1933), which was originally termed "influenza virus" or "human influenza virus" and more recently "epidemic influenza virus." If and when other "influenza viruses" are isolated from patients they could be labelled influenza B virus, C virus . . . . &c., to correspond with the diseases influenza B, C, ... &c.

Influenza-like diseases attacking primarily animals other than man (e.g., swine influenza) should be excluded from the A, B, C, ... terminology.

Confusion might arise if two independent groups of workers were to give the same letter to different viruses (such confusion is not unknown in the sphere of vitamins); or a letter might be bestowed on a virus whose status was subsequently rendered doubtful. It is suggested, therefore, that influenza viruses before being "christened" should be submitted for study either to the Rockefeller Institute or to the National Institute for Medical Research.

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SURVIVAL OF STORED RED CELLS AFTER TRANSFUSION

BY

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WHEN a transfusion is given for anæmia, the important element in the blood is the red cell ; likewise, with severe hæmorrhage a transfusion is often designed theoretically to restore red-cell elements so that oxygen-carrying power may be increased. But with acute hæmorrhage and more especially with wound shock there are other more important advantages to be gained from transfusion ; these include restoration of blood volume, blood protein, and a reasonable blood-pressure ; with such advantages this paper is not greatly concerned. In preparation for extensive battle and air-raid casualties both the military and the civil authorities established organisations for supplying blood in large quantities. In the waiting period this stored blood was much used for ordinary civil practice, and at the same time research was concentrated on the finding of diluents, anticoagulants, chemicals, and other factors designed to ensure that the red cells would, for long periods, be sufficiently well preserved to survive in a recipient when transfused. This survival of the red cells is clearly of great importance in many of the medical cases of civil practice ; but for shock and acute hæmorrhage restoration of blood volume is more vital than oxygen-carrying power.

It was early noted by us that every transfusion of blood (to which, at that time, no glucose was being added) stored for more than two days caused a detectable increase in plasma bilirubin, even though no clinical jaundice was apparent. With large 3-pint drip transfusions an increase in plasma bilirubin was detectable even with two-day-old blood. This increase in plasma bilirubin was not due to free hæmoglobin in the transfused specimen, for none was ever obvious, and free hæmoglobin is rapidly excreted unless it is fairly concentrated. We found by experiment that transfusion of a volume of blood containing less than 3 g. of free hæmoglobin produced a detectable rise in plasma bilirubin, whereas the intravenous administration of 3 g. of free hæmoglobin to a normal man caused no such rise. These results suggested that rises in plasma bilirubin were due to in-vivo hæmolysis of transfused cells, and that the circulating pigment was derived from fragile cells contained in the transfused specimen.

The rise in plasma bilirubin was usually maximal about four hours after the transfusion of a pint of blood (occupying about twenty minutes), and had always declined very much by the end of twenty-four hours. Table I gives examples of these findings and shows the advantage of adding glucose to stored blood.

The only true test of whether transfused red cells endure in the recipient is to follow the fate of the cells by repeated examinations. For this purpose a simple blood-count is insufficient, because it does not show whether rises or falls in a total count are due to autogenous cells or to the transfused blood. But when group-O blood is transfused to a group-A or group-B patient, or when group-"M" blood is transfused to a group-"N" patient and vice versa, the fate of the transfused blood can be observed by the method described by Ashby (1921)—namely, by making counts of the cells not agglutinated by an appropriate serum. With ABO determinations, the non-agglutinated cells, except a number which is roughly constant for each case and can be determined, represent the transfused cells. These can be followed from day to day and even from hour to hour. We have studied the fate of stored blood of different ages by

TABLE I—QUANTITATIVE VAN DEN BERGH ESTIMATIONS AFTER TRANSFUSION OF 1 PINT OF BLOOD

—	Age of blood (days)	van den Bergh units		
		Before	In 4 hours	In 24 hours
Without glucose	5	0·50	3·00	0·75
	12	0·50	8·00	0·75
	18	0·25	9·00	1·00
With glucose	7	< 0·25	0·25	< 0·25
	12	< 0·25	4·00	1·00
	19	0·25	3·50	2·00
	36	0·25	3·00	1·50

the Ashby technique, and, from the results obtained with blood containing glucose and with blood containing no glucose, we have deduced that the in-vitro physical property of fragility is an index of the ability of the cells to endure in vivo. We have therefore used the quantitative fragility test as a criterion for assessing the value of a number of chemicals, diluents, preservatives, and other factors designed to prolong the period of preservation of red cells.

SURVIVAL OF TRANSFUSED CELLS

The technique employed was to transfuse group-O blood to a group-A or group-B patient. Counts of the recipient's blood were taken at intervals (table II), a 1 in 101 dilution being made with the appropriate α or β serum ; the titre of the sera so used was 1 in 320. After being thoroughly mixed in the pipette, the contents were immediately expelled into a corked tube and incubated at 37° C. for an hour, being shaken at intervals of fifteen minutes. At the end of this time a drop was placed on a counting chamber and a count made of the "free" non-agglutinated cells, which represent transfused group-O cells. Before transfusion the "non-agglutinable count"—i.e., the number of A or B cells not agglutinated by the particular α or β serum—was determined in each

patient. This number, which is assumed to be constant for each person, is subtracted as a correction from the "free"-cell count before the number of surviving group-O cells is calculated. With the sera used by us the "non-agglutinable count" was 50–100,000 per c.cm. During these investigations we observed that reticulocytes were agglutinated in the same manner as mature cells; this is contrary to the statements of Isaacs (1924). The

TABLE II—SURVIVAL OF TRANSFUSED GROUP-O CELLS (WITHOUT GLUCOSE)

Age of blood	Percentage of transfused cells surviving (days)					Final examination day/% surviving	Hæmolysis % in NaCl %					Hæmolysis
	1	2	3	4	5		0·5	0·55	0·6	0·65	0·7	
1	100	100	100	100	90	20/65	tr.	0	0	0	0	Nil
2	100	100	100	100	100	5/100	15	10	5	tr.	tr.	,,
3	100	90	90	85	80	20/58	30	10	tr.	,,	0	,,
4	80	80	80	80	80	25/40	20	10	5	,,	0	,,
5	100	95	—	—	—	—	5	tr.	tr.	,,	tr.	,,
5	100	70	60	50	50	5/50	20	15	5	5	,,	,,
5	100	90	90	85	80	5/80	10	tr.	tr.	0	0	,,
6	80	70	70	70	70	25/30	10	5	,,	tr.	0	,,
6	70	60	55	45	40	5/40	35	20	10	,,	tr.	< 1%
7	60	40	35	30	30	15/15	30	30	15	5	,,	< 1%
8	80	70	50	45	40	6/35	50	30	20	10	,,	< 1%
10	24	24	15	10	10	5/10	70	60	50	40	20	< 1%
10	40	35	30	25	20	5/20	80	70	60	30	30	1%
12	10	0	0	0	0	5/0	90	80	50	30	30	3%
16	80	50	24	18	12	9/0	60	50	50	50	40	6%
19	20	15	10	8	6	5/0	80	70	60	60	60	12·5%

cases included in tables II and III were largely of bleeding from the alimentary canal; old hospital patients with chronic disease, such as rheumatoid arthritis with anæmia, who volunteered to be subjects; and a few cases of non-hæmolytic blood diseases. So far as could be determined, bleeding had ceased in all hæmorrhagic cases.

Tables II and III show the percentage of cells surviving up to five consecutive days and for times up to twenty-five days, besides the quantitative fragility test of the transfused sample and the amount of hæmolysis present in it. The two tables demonstrate clearly the superior survival-rate and the superior fragility tests of the red cells of blood ten or more days old when preserved with glucose. The blood samples recorded in table II consisted of 100 c.cm. of a 3% solution of sodium citrate, 440 c.cm. of blood, and 40 c.cm. of a 0·85% saline solution; those in table III contained 40 c.cm. of a 5% solution of glucose instead of the saline solution, and this is now the routine anticoagulant used in the Army Transfusion Service. Fig. 1 shows graphically the facts concerning some of the cases recorded in tables II and III and emphasises the superiority of glucose-containing blood.

Fig. 2 shows the correlation between survival for a day and three days and the fragility to a 0·55% saline solution. The sources of error in the experimental method are considerable and probably amount to 20%. Among the various errors which arise are inaccuracies in counting; these are increased by the difficulty of deciding whether pairs of cells are the result of agglutination or of random settling, and whether large agglutinated clumps are obscuring free cells. Further, with aged blood the destruction of cells begins during transfusion; hence it is impossible to determine the number of cells transfused. This last error is greatly increased when a large transfusion is given slowly. In these circumstances the correlation between fragility and survival, which to be exact should show all points lying on a straight line, can be considered good and certainly good enough to indicate that fragility and cell survival are closely related. Tables II and III show that, although glucose decreases crude hæmolysis, absence of hæmolysis—e.g., less than 1% in thirty-six-day-old blood—does not necessarily imply long survival. Hæmolysis in the sample is not, therefore, a good index of cell survival.

INFLUENCE OF VARIOUS FACTORS ON THE FRAGILITY TEST OF STORED BLOOD

As a rule samples of blood have been examined for fragility and other tests have been applied after storage for seven, fourteen, and twenty-one days. In investigating any one particular factor, it is important that the samples tested at the above intervals be derived from the same donor. It is convenient, therefore, to collect blood for such tests into 30 c.cm. screw-cap bottles containing anticoagulant in the right proportions. This provides plenty of material for duplicate tests and allows many different tests to be performed at the expense of only one donor. It also ensures that a sample removed for test, say, at seven days has not to be examined and then again stored for further examination at fourteen days; an undisturbed sample is available for each test at the stated interval.

The following substances have been investigated for their influence on the fragility of stored blood. For economy in space the facts are categorically stated unsupported by the lengthy protocols of the vast number of quantitative fragility tests (Creed's method) on which the conclusions are based.

Carbohydrates.—All workers are agreed that glucose helps in the preservation of red cells. Tables II and III and figs. 1 and 2 clearly show the beneficial effect on survival and on fragility. The optimal final concentration of glucose is 0·25–0·50%. A final concentration as high as 1% is not so good, and concentrations less than 0·125% are even less so. It is the final concentration that is important and not the manner whereby this is obtained. For instance, it is immaterial whether a 5% or a 50% solution is added to the blood, so long as the final concentration is 0·25–0·50%. It is also immaterial whether glucose is added before the blood is taken or at any time within twenty-four hours of collection. Red cells which have become fragile cannot be reconditioned by the addition of glucose. Lævulose is as effective as glucose; saccharose (0·25–5·00%) and dextrin (2·5–16·0%) are slightly inferior; glycerol (1·5%) is definitely deleterious.

Citrate and other anticoagulants.—Experiments have shown that the strength of sodium citrate can vary from 2% to almost 4% without affecting the ultimate fragility test. Nevertheless, a 3% solution, judging from empirical observations, is as nearly isotonic with blood as can be attained. Strengths of 6% and 10% definitely increase fragility. It is immaterial whether the sodium or the potassium salt is used. Heparinised blood does not preserve so well as citrated blood; but, if the donor

TABLE III—SURVIVAL OF TRANSFUSED GROUP-O CELLS (WITH GLUCOSE

Age of blood	Percentage of transfused cells surviving (days)					Final examination day/% surviving	Hæmolysis % in NaCl %					Hæmolysis
	1	2	3	4	5		0·5	0·55	0·6	0·65	0·7	
5	90	90	90	90	90	12/90	30	10	tr.	0	0	< 1%
7	90	90	80	80	80	23/55	80	30	10	tr.	0	< 1%
8	80	70	70	65	60	5/60	90	30	tr.	0	0	Nil
11	86	75	70	65	60	5/60	60	30	10	tr.	0	,,
12	80	80	80	70	60	25/44	60	30	10	5	tr.	1%
14	70	65	60	60	60	8/30	80	40	30	20	10	Nil
16	90	85	80	—	—	—	80	40	30	15	<10	< 1%
19	80	50	50	50	50	5/50	50	40	15	10	tr.	< 1%
24	40	30	30	24	24	25/18	50	40	20	10	0	< 1%
36	60	40	30	25	20	14/0	80	60	50	30	20	< 1%

is heparinised and the blood received into citrate solution, the period of preservation is unaffected.

Dilution and plasma factors.—Fragility is greatly improved by dilution of the blood. This suggests that plasma factors are concerned in the deterioration of red cells during storage. For this view there is some experimental evidence in that substitution of plasma with a 3% solution of sodium citrate prolongs the period of preservation; but if physiological saline is used to replace plasma, the period of preservation is reduced.

Plasma does not appear to alter in tonicity on storage up to fifty days. Further, fresh cells suspended in plasmas of different ages are neither better nor worse preserved than in their own plasma. Blood diluted with equal parts of a 3% solution of sodium citrate is much better preserved than when it is diluted with 100 parts of the solution of sodium citrate to 440 parts of blood, as is usually done in the Army Transfusion Service. Dilution appears to be the only virtue in the complicated I.H.T. (Bagdassarov 1937) fluid which was used in equal

parts with blood. When blood is excessively diluted, there is the disadvantage that the red-cell content of the transfused specimen is proportionately low.

Saline.—Physiological saline, unlike a 3% solution of sodium citrate, is a worse storage medium than plasma; and, when saline is added to an isotonic solution of sodium citrate, the period of preservation is shortened. The anticoagulant recommended by Harrington and Miles (1939) and widely used contains physiological saline and is definitely inferior to a simple 3% solution of sodium citrate (in the proportions of 100 c.cm. of solution to 440 c.cm. of blood), even though there is the compensating advantage given by the increased dilution in which this anticoagulant is ordinarily used—namely, 180 c.cm. of anticoagulant to 360 c.cm. of blood.

Temperature.—Storage of blood at 37° C., at room temperature (18°–22° C.), and at − 1·5° C. is definitely deleterious compared with storage at 4°–6° C. Rapid cooling of the blood after collection does not decrease fragility, even if the blood is received immediately into a cooled vessel. Other variations of this theme have been found to have no advantage. Undue delay (twenty-four hours) in refrigeration is deleterious; cooling to 0° C. for two days before storing at 4° C. has no effect; and warming to room temperature after four days at 4° C. has no adverse action. This last fact shows that

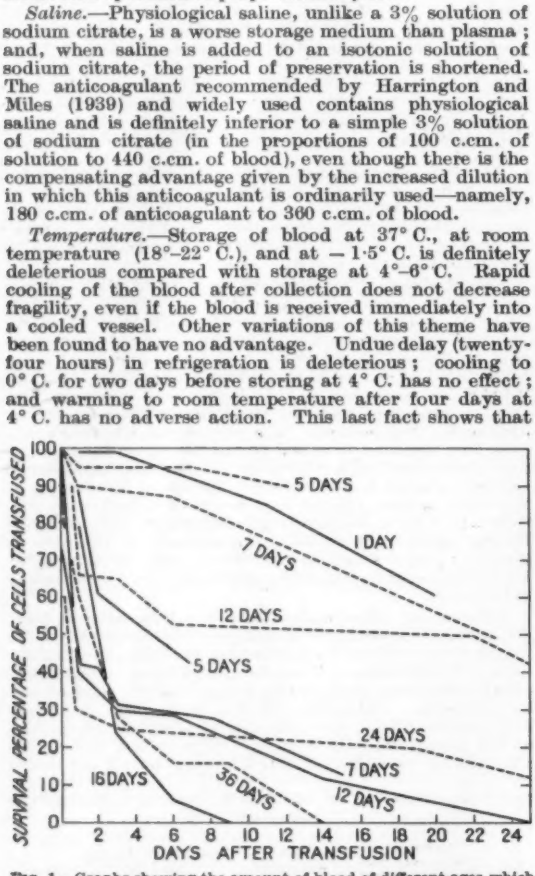

FIG. 1—Graphs showing the amount of blood of different ages which survives transfusion for a given time. The age of the blood is stated against each graph. Interrupted lines, glucose-containing blood.

it is possible to remove a bottle of sterile blood from the refrigerator, warm it up, and then store it again without detriment.

Acidification.—The pH of the Army blood mixture is ordinarily 8·6. The addition of buffer solutions is either deleterious or ineffective, but acidification with citric acid to pH 5 was found to improve fragility almost as much as did the addition of glucose. This effect with citric acid does not greatly enhance the action of glucose (fig. 3). The optimal action does not appear to be so much an adjustment of the pH of the anticoagulant as the addition of sufficient acid to overcome the buffering action of the blood and so alter its pH. The effect is independent of the citrate anticoagulant, for it can be demonstrated in heparinised blood, and it can be obtained by adding acids other than citric acid—e.g., hydrochloric acid and acetic acid. Acidification appears to retard glycolysis, and this is perhaps the reason for the beneficial action.

Though acidification prolongs the period of preservation of red cells and has the distinct additional advantage, when citric acid is added to sodium citrate, that the sodium citrate can then be autoclaved with glucose without caramelisation, it has been found by animal experiment that blood so acidified appears to have toxic properties. This is therefore not carried out in practice.

Oxygenation.—Saturation of blood with oxygen or the addition of hydrogen peroxide (2% of 10 volumes) improves the appearance of blood as well as the fragility

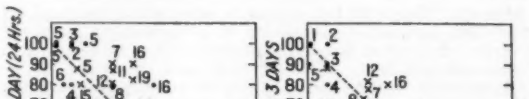

FIG. 2—Correlation between fragility to 0·55% saline solution and percentage of cells surviving one day and three days. The age of the blood is stated against the plotted points. Samples containing glucose are marked x.

in the early stages of storage (seven days), but the period of preservation is not prolonged by such treatment. With a view to designing the ideal container for the storage of blood, investigation was made to find whether there was any difference between the preservation of a thin layer of blood with a large surface exposed to air (2 c.cm. of blood in a 250 c.cm. flat bottle laid on its side and a thick layer with a small exposed surface (5 c.cm of blood in a 5 c.cm. bottle). No difference was detected.

Enzymes and leucocytic action.—Neither the addition of substances known to inhibit enzyme action nor the removal of sources of enzymes appears to have any action. Red corpuscles removed from the lowermost parts of a conical centrifuge tube contain no leucocytes; these red corpuscles when resuspended in the supernatant plasma are no better preserved than those of complete blood. Of substances known to inhibit enzyme action neither potassium fluoride nor potassium cyanide nor formalin has any beneficial effect on storage.

Sundries.—The following substances have either no action or else a deleterious action on blood storage: cholesterol, lecithin, formalin, unicol, phenates of sodium, tragacanth, and gum arabic (5% solution). It is perhaps noteworthy, in view of the division of opinion about gum saline, that when plasma is removed and red cells are resuspended in a 5% solution of gum arabic, hæmolysis of the cells is rapid.

COMMENTS

It is clear that, when blood is collected into a 3% solution of sodium citrate in the proportion of 100 c.cm. of citrate to 440 c.cm. of blood and stored at 4°–6° C., the following substances or procedures prolong the period of preservation of the red cells, as judged by a quantitative fragility test: adjustment of pH to 5 (of no value in practice), dilution, and addition of glucose. The effect of these various factors and their cumulative action are shown in fig. 3, which sets out the quantitative fragility tests of a sample of blood after twenty-one days' storage under the single and combined conditions. Of the single factors, glucose (curve 4) is outstandingly the best. The enhancement given by glucose and dilution (curve 5) or

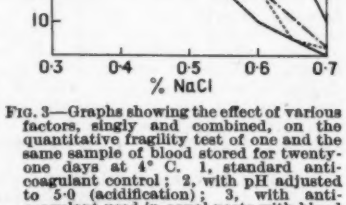

FIG. 3—Graphs showing the effect of various factors, singly and combined, on the quantitative fragility test of one and the same sample of blood stored for twenty-one days at 4° C. 1, standard anticoagulant control; 2, with pH adjusted to 5·0 (acidification); 3, with anticoagulant used in equal parts with blood (dilution); 4, with 0·3% solution of glucose; 5, with glucose + dilution; 6, with glucose + dilution + acidification.

by glucose + dilution + acidification (curve 6) is recognisable as such, but the degree is not sufficient to justify utilisation for practical storage of blood.

For the acute hæmorrhage and shock of the wounded the prime necessity is to restore blood volume adequately. This is more vital than elevating oxygen-carrying power to a high level, for those who survive an acute hæmorrhage rarely die later from lack of oxygen-carrying power. Moreover, with restoration of blood volume the efficiency of such oxygen-carrying elements as have not been lost by hæmorrhage is automatically increased.

Brewer et al. (1940) have reported that stored blood (containing glucose) ten to fourteen days old is as efficient as fresh blood for the treatment of acute hæmorrhage. Our survival figures confirm this statement and show that even older blood survives a reasonable time in the recipient and certainly long enough to keep a wounded man alive until he arrives at a point where he can receive complete surgical treatment. Such was indeed the experience in recent campaigns, during which some five hundred transfusions were given of blood ten to thirty days old. Further, this old blood appeared to have a negligible incidence of reactions, even though it had been subjected to the batterings incidental to transport. This good preservation may have been partly due to the Army system of " topping " the bottle so that it is completely filled, all air excluded, and no slopping possible. De Gowin et al. (1940) found that hæmolysis was delayed when blood was stored in sealed air-displaced flasks, as compared with blood exposed to air. It is clear from the bilirubinæmia which is associated with the transfusion of stored blood that the older the blood the more rapidly are its fragile corpuscles destroyed. The iron pigment thus set free is phagocyted by the reticulo-endothelial system and assists in blood regeneration during convalescence from hæmorrhage. Provided that blood is not so old as to liberate too suddenly a dangerous quantity of pigment, the transfusion of even quite old blood to the exsanguinated has much to commend it.

In carrying out the vast amount of onerous, even boring, work which this paper represents we have had the loyal support of all the staff of the Army Blood-Transfusion Service, to whom our thanks are due. We wish to mention especially the help of Lieutenant Ethel Whitby, Lieutenant Joan Parry, Lieutenant Faith Poles, Lieutenant Joyce Morgan, and Staff-Sergt. R. Blake, of the R.A.M.C., and volunteers S. Kekwick and D. E. Vaughan-Jones, of the A.T.S. One of us (A. K.) gratefully acknowledges financial support from the Leverhulme Trust both before the war and since.

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SURVIVAL OF STORED BLOOD AFTER TRANSFUSION

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THE establishment of so-called blood banks during the present war has focused attention on the use of stored blood in the treatment of hæmorrhage. There are several ways in which the value of stored blood may be investigated : by clinical observation ; by the increase in the recipient's hæmoglobin brought about by transfusion and the permanence of this rise ; and by the direct demonstration of the persistence of the donor's cells in the circulation of the recipient. There are certain difficulties in the way of the first two methods : clinical investigations require a large series of cases and minute observations ; and the hæmoglobin level after transfusion is affected by numerous factors, including further hæmorrhage and dilution of the recipient's blood. On the other hand, the degree of persistence of the donor's cells after transfusion affords the most direct and positive evidence of the value of transfusion of stored blood. This third method was adopted in this investigation, which deals with the survival of stored blood-cells measured with iso-agglutinins and of changes in the chemistry of stored blood-cells in the recipient's blood after transfusion. Transfusions have been carried out with blood and citrate solution mixed in the proportion of 2 to 1. The citrate solution contained sodium citrate 1·05%, sodium chloride 0·85%, and glucose 3%.

SURVIVAL OF STORED BLOOD-CELLS MEASURED WITH ISO-AGGLUTININS

Ashby (1919) devised a method of measuring the survival of erythrocytes after transfusion of fresh blood by using group-O donors for group-A recipients. Blood was withdrawn from the recipient before transfusion and at suitable intervals afterwards and mixed with group-B serum. The recipient's (A) cells were agglutinated while the donor's (O) cells remained free and were counted. It was assumed that the number of free cells present at any given interval after transfusion represented the number of transfused cells surviving at that time. This method has been successfully applied to the transfusion of fresh blood by other workers (Wearn et al. 1922) and has been adapted to give rough quantitative results with M and N cells and antisera by Landsteiner et al. (1928) and Dekkers (1939).

We have applied this method to the measuring of the survival of stored blood and have simplified the technique by passing the mixture of agglutinated (A) cells, free (O) cells, and group-B serum through a filter paper. The agglutinated cells are retained by the filter. The free cells pass through and are easily counted. Although the technique of counting inagglutinable cells in unfiltered preparations is not difficult to acquire, filtration removes many irrelevant cells from the microscope field and makes counting quicker and easier.

Method.—20 c.mm. of the recipient's blood (in a hæmoglobin pipette) is mixed with 1·5 c.cm. of a solution containing sodium citrate 1·05% and sodium chloride 0·85%, and then 1·5 c.cm. of group-B serum is added. The serum must have a very high agglutinating titre (1/256 or more), because low titres give inaccurate results. The mixture of cells and serum is poured into a beaker (150 c.cm.) so as to form a thin layer on the bottom. This aids agglutination. After standing for two hours at room temperature the cell suspension is thoroughly mixed by rotation without shaking and poured through a filter paper (Whatman No. 4). It is important that the paper should fit the funnel snugly. The first seven or eight drops are collected and counted in the ordinary way. Occasionally, very small agglutinated masses pass through the filter paper. These and even pairs of cells in contact are rejected, so that only free single cells are included in the count. If many small agglutinates are found in the filtrate, it is probable that the titre of the agglutinating serum is too low. These low-titre sera do not agglutinate completely, even when mixed with cells possessing the appropriate agglutinogen, and the system resulting contains small agglutinates, paired cells, and single cells, most of which would be agglutinated by sera of higher titre. These high-titre sera not only agglutinate almost completely but also produce agglutinates of such consistently large size as to be completely retained by the filter paper. A good agglutinating anti-alpha serum when mixed with A cells shows 0·02–1·00% of unagglutinated cells—usually about 0·30%.

Errors, then, may arise from single A cells filtering through along with the O cells giving high results, and they may also arise from some of the donor's O cells being caught up in the mass of the recipient's cells or

in the filter paper. This would tend to give low results. It follows, therefore, that the type of filter paper used is of importance. Our experiments were done with Whatman No. 1 of pre-war manufacture, and it was concluded that filtration did not introduce any serious inaccuracies in the cell counts, because duplicate experiments gave comparable results, whereas imitation of these counts with known amounts of O cells, A cells, and B serum in the right proportions mixed in vitro showed that over 80% of the theoretical number of O cells was recovered after infiltration. Thus, when 20 c.mm. of blood containing 5,000,000 A cells and 300,000–400,000 cells per c.mm. was mixed with 3 c.cm. of the diluted B serum and filtered, the percentage recovery and standard deviation in seventeen experiments was 87 ± 6; if A cells were kept at 5,000,000 and O cells were reduced to 175,000 per c.mm., recovery was $88 \pm 8\%$; and, when O cells were only about 90,000, recovery was $92 \pm 9\%$. It appeared, then, that pre-war Whatman No. 1 was very satisfactory, but the use of war-time Whatman No. 1 (which is made of different materials) gave a recovery averaging only about 70% (range 62–85%). This batch of Whatman No. 1 is therefore unsuitable for the special purpose, but war-time Whatman No. 4, which gives a recovery of 90%, is quite suitable. Roughly speaking, the percentage of cells recovered is proportional to the speed of filtration. Thus six pre-war Whatman No. 1's delivered 0·5 c.cm. in $14·3 \pm 1·5$ sec. from the time that the cell suspension was poured into the funnel; war-time Whatman No. 1 took 29 ± 3 sec.; and war-time Whatman No. 4 took only $4·5 \pm 0·5$ sec. Papers from these three batches gave 81, 62, and 89% recovery respectively. It is therefore suggested that experiments should be rejected in which filtration of 0·5 c.cm. takes more than 16 sec.; this is very unlikely to happen when pre-war Whatman No. 1 or war-time Whatman No. 4 is used. Further evidence in favour of these views is given in table I, in which are set out duplicate experiments showing the percentage recoveries

TABLE I—RECOVERY OF O CELLS FROM FILTRATES OF A CELLS, O CELLS, AND B SERUM MIXED IN VITRO

A cells in mixture before filtration per c.mm.	O cells in mixture before filtration per c.mm.	Net recovery of O cells after filtration %					
		Whatman No. 1 pre-war		Whatman No. 1 war-time		Whatman No. 4 war-time	
		a	b	a	b	a	b
0	260,000	97	90	74	70	96	84
5,200,000	260,000	102	87	75	66	95	85
5,200,000	130,000	86	87	70	68	89	94
5,200,000	65,000	96	94	71	75	88	82

of O cells filtered through pre-war and war-time Whatman No. 1 and war-time Whatman No. 4. It should be remembered that the figures in the two left-hand columns of the table refer to cells per c.mm. of original blood. Since 20 c.mm. of this blood was suspended in 3 c.cm. of a citrate-saline-serum mixture, the number of cells in the suspension is a hundred and fifty times less. Cell recovery after filtration of such suspensions was $90 \pm 10\%$.

Criticism of method.—In spite of the success attending the use of Ashby's method by several workers, Isaacs (1924) has levelled certain criticisms against the whole technique. It may be said at once that these criticisms are theoretical and are unsupported by numerical data. However, since the cell-agglutination technique is the only one which permits of a direct measure of cell survival, the objections must be considered in detail.

Isaacs points out that previous workers have found that, when group-A cells alone (without O cells) are mixed with B serum, there is a small residue of inagglutinable cells. In our work this inagglutinable residue usually amounts to about 20,000 cells per c.mm. of blood and constitutes a "blank" value which must be taken into consideration when counts are made after transfusion with O blood. Thus in table I the blank values have been subtracted from cell counts to obtain the net number of O cells in the filtrate. Isaacs says that this blank consists of immature erythrocytes (reticulocytes) normally present in the circulation, and that it is these immature cells which are inagglutinable. He also says that transfused blood, even when freshly drawn, is rapidly destroyed after transfusion, and that this evokes a reaction similar to that which takes place when the recipient's cells are rapidly removed from the circulation by whatever means—namely, the appearance of immature cells. It is this shower of immature cells which is said to be inagglutinable and not the donor O cells.

In Isaacs' paper there is very little evidence in favour of this view. He admits that two of his human cases showed no immature cells after transfusion; in two other cases a reticulocytosis is shown in accompanying graphs, but numerical data are not supplied. On the other hand, there are many serious objections, which may be summarised as follows:—

(1) If rapid destruction of transfused erythrocytes evokes a response of immature inagglutinable cells, there should be a higher inagglutinable cell count with old blood than with fresh blood, because old blood will be more rapidly broken down; but in fact the counts are lower.

(2) If the appearance of inagglutinable cells is evoked by the destruction of transfused cells, then transfusion from an A donor to an A recipient should give as high an inagglutinable cell count as transfusion from an O recipient to an A donor; but this is not so. According to Ashby (1924) transfusion of A blood to an A recipient caused sometimes a slight increase in the blank and sometimes a decrease.

(3) If the inagglutinable cells are immature, the filtrate from the recipient's blood after transfusion and agglutination should show a high reticulocyte count, and certainly a higher count than the bulk of the recipient's cells before agglutination with B serum; but the reverse is the case: the filtrate was devoid of reticulocytes in fourteen observations on six cases, and the recipient's whole blood contained 0·1 to 3·0 of reticulocytes.

(4) Whereas human erythrocytes may either possess iso-agglutinogens A, B, or AB or else no agglutinogens at all (O), they always possess hetero-agglutinogens—M, N, or MN. Hence, provided that the donor's and the recipient's cells have different hetero-agglutinogens, their separate identities should be demonstrable after transfusion. If, for example, OM blood is given to an ON recipient and the recipient's blood is tested later, anti-M serum should show many free (recipient's) cells and a few agglutinated masses (donor's cells); if anti-N serum is used, the recipient's blood will show many agglutinated (recipient's) cells and a few free (donor's) cells. This method has been used by Dekkers (1939), who finds that, after the transfusion of fresh blood, donor's cells survive for many weeks in the circulation of the recipient.

It therefore seems that Isaacs' theories must be rejected, and that, when a recipient's (A) cells are mixed with B serum, the inagglutinable cell count before transfusion is due to the presence of recipient's cells containing insufficient agglutinogen to react with the agglutinins, and that the inagglutinable cell count after transfusion is due to the presence of these same cells plus the inagglutinable O cells of the donor. Theoretically, therefore, to obtain the true count of O cells surviving after transfusion, the blank value of recipient's A cells deficient in alpha agglutinogen should be subtracted from the total inagglutinable cell count. Unfortunately, the true blank value at the time of each observation cannot be known, and it may well differ from the original blank before transfusion. Indeed, it is possible that blanks vary in normal people from time to time, and this is more likely to happen in anæmic patients under treatment. In such people the red cells may double and the whole blood-count alter in a few weeks. There is no information as to whether the blank value changes in proportion.

For these reasons total inagglutinable cell counts only are shown in table II. To obtain a rough idea of the number of transfused cells surviving, it is simplest to subtract a maximal probable blank value of 50,000 cells from the total inagglutinable cell count. Since the blank is usually 10,000–50,000, subtraction of the latter figure will give, in all but a few cases, a value which equals or is slightly less than the number of donor's cells surviving after transfusion.

If the data in table II are interpreted in this way the following observations may be made. Patients may be

TABLE II—INAGGLUTINABLE CELL COUNTS

Case	Age of stored blood (days)	Inagglutinable cell count per c.mm.											
		Before transfusion (blank)	Days after transfusion										
			1/12th	3	6	9	15	21	28	35	42	49	63	84
1	1	17,000	580,000	570,000	475,000	360,000	..	..	..	..	..	..	..	..
2	2	150,000	560,000	..	475,000	..	..	..	..	..	..	..	..	..
3	6	20,000	350,000	365,000	..	267,000	245,000	..	288,000	221,000	..	176,000	123,000	28,000
4	7	120,000	930,000	..	880,000	..	..	..	..	..	..	..	..	..
5	7	12,000	290,000	360,000	290,000	290,000	..	280,000	150,000	150,000	166,000	..	..	61,000
6	7	34,000	545,000	387,000	410,000	355,000	355,000	344,000	186,000	..	..	152,000	152,000	..
7	8	50,000	850,000	650,000	810,000	..	385,000	359,000	..	290,000	280,000	272,000	102,000	..
8	8	40,000	380,000	272,000	248,000	..	198,000	..	..	..	..	..	..	..
9	8	4000	275,000	..	234,000	..	..	..	..	..	..	..	..	..
10	12	20,000	420,000	408,000	376,000	..	425,000	205,000	..	227,000	198,000	130,000	42,000	..
11	13	16,000	306,000	297,000	297,000	..	284,000	297,000	..	..	..	..	..	..
12	14	10,000	630,000	360,000	290,000	310,000	..	..	..	..	..	..	..	..
13	14	20,000	530,000	452,000	450,000	..	..	229,000	..	..	..	..	..	..
14	14	12,000	320,000	..	186,000	..	138,000	173,000	112,000	..	..	..	..	..
15	15	20,000	320,000	212,000	210,000	190,000	..	192,000	..	..	..	167,000	119,000	118,000
16	15	10,000	250,000	62,000	50,000	..	..	..	..	..	..	..	..	..
17	15	24,000	340,000	140,000	150,000	..	109,000	..	110,000	95,000	..	72,000	..	27,000
18	16	14,000	226,000	240,000	185,000	..	..	..	..	..	..	..	..	..
19	19	87,000	240,000	222,000	154,000	..	164,000	..	..	..	..	..	..	..
20	19	10,000	270,000	249,000	230,000	237,000	..	..	..	..	..	..	..	..
21	21	20,000	200,000	38,000	28,000	..	..	..	..	..	..	..	..	..
22	21	60,000	220,000	220,000	180,000	..	..	..	..	..	..	..	..	..
23	21	26,000	80,000	72,000	34,000	..	..	..	..	..	..	..	..	..

divided into three groups ; those receiving blood less than a week old, those receiving blood between one and two weeks old, and those transfused with blood more than two weeks old. In the first group, when the donor's blood was less than a week old, more than 75% survived six days after transfusion, and more than 66% was still present fifteen days afterwards.

In the second group, where cells were stored for seven to fourteen days, more than 75% of cells survived after six days and 45–100% were still present fifteen days after transfusion.

In most cases the count of transfused cells declined some time in the first fortnight. The counts remained fairly constant during the third week but thereafter again gradually declined. However, in some instances transfused cells were still found months after transfusion.

In the third group of cases receiving blood stored for more than a fortnight the data are scanty. There was a rapid fall in the agglutinable cell count in the first three days after transfusion in cases 15, 16, 17, and 21, and by the sixth day in cases 19 and 23. In cases 15 and 16 cell destruction was very noticeable during the first three days, but after this it was much slower, and in case 15, as in case 5, there was evidence that transfused cells were still surviving after eighty-four days. The inagglutinable cell counts in these two cases were checked by using two different sera of titres 1/512. The low count after transfusion in case 23 suggests that the cells were being rapidly destroyed even during the transfusion. Even normal blood contains many aged erythrocytes, and rapid destruction of these must be expected even after the transfusion of fresh cells. It seems possible that the rapid initial fall in the number of transfused cells for stored blood may be due to the destruction of effete corpuscles, and that those that do not quickly succumb are relatively resistant to hæmolysis. It has only been possible for us to check our results with hetero-agglutinating sera (anti-M and anti-N) in one case (No. 16) here thirty-five days after transfusion, the bulk of the recipient's cells were agglutinated by both anti-M and anti-N ; the cells in the filtrate after preliminary agglutination with B serum reacted only with anti-M serum and not with anti-N. In this instance, then, the existence of two races of cells in the recipient's circulation was demonstrated thirty-five days after transfusion by iso- and hetero-agglutination.

SODIUM CONTENT OF STORED CELLS AFTER TRANSFUSION

It has been shown (Maizels and Whittaker 1940) that stored erythrocytes often contain more than four times as much sodium as do fresh cells. Since it is known that stored cells survive for many days after transfusion, it was thought of interest to measure what changes took place in the chemistry of the donor's cells after they had reached the recipient's circulation.

Method.—The specimens were centrifuged for fifteen minutes at 3000 r.p.m. The supernatant plasma and upper face of the erythrocyte columns were removed with a capillary pipette. The residues were recentrifuged, and any remaining trace of plasma was finally removed. 0·5 c.cm. of cells was ashed in platinum crucibles and the ash taken up in 2 c.cm. of water to which was added 0·1 g. of calcium hydroxide. The contents of the various crucibles were centrifuged in pyrex tubes, 1 c.cm. of the clear supernatant solutions and 1 c.cm. of each of the four dilute standards placed in other tubes, and the sodium contents estimated by precipitation with zinc uranyl acetate according to the method of Salit (1932) slightly modified.

In plasma, where the Na/K ratio is high, Salit's method gives accurate results, but human erythrocytes have a very low Na/K ratio, and in our experience this method gives results which are too high, and the zinc uranyl acetate precipitated from ashed cells contains a high proportion of potassium, at least under conditions of temperature found in England during winter and spring. Precipitation of sodium with little or no potassium was obtained if to 1 c.cm. of the cell extract and the diluted standards were added 2·3 c.cm. of Salit's zinc uranyl acetate reagent, 0·7 c.cm. of water, and 0·55 c.cm. of alcohol.

After standing for forty-five minutes, the tubes were centrifuged and the precipitates washed with alcohol saturated with sodium zinc uranyl acetate. The precipitates were then taken up in 50 c.cm. of water; 0·2 c.cm. of glacial acetic acid and 0·5 c.cm. of potassium ferrocyanide (20%) were added. The various unknown samples and the three other standards were compared with the remaining standard in a colorimeter, and the final results were worked out from the calibration curve obtained.

Samples containing known amounts of sodium within ± 50% of the standard show results in good agreement with the theoretical values. Figures outside this range must be obtained by reference to the calibration curve. This curve is fairy reproducible, the data usually being approximately as follows (table III).

TABLE III—ESTIMATION OF SODIUM
Standard = 80 mg.%

Theoretical value (mg.%)	Colorimetric value (uncorrected)
16	21
48	51
80	80
112	104

The strong standards contain 100, 300, 500, and 700 mg.% respectively. For use, these strong standards are diluted twenty-five times.

TABLE IV—SODIUM CONTENT OF STORED CELLS AFTER TRANSFUSION

Case	No. of days stored	Blood	Sodium content of cell (mg. per 100 c.cm.)	Icterus index	Inagglutinable cells per c.mm.
1	3	Donor's	80·0	..	..
		Recipient's before transfusion	40·6	2·5	..
		,, 2 hours after transfusion	47·6	2·5	..
		,, 24 ,, ,, ,,	39·1	2·5	..
2	3	Donor's	..	..	..
		Recipient's before transfusion	30·0	..	..
		,, ½ hour after transfusion	46·0	..	..
		,, 24 hours ,, ,,	29·0	..	550,000
3	5	Donor's	101·0	..	..
		Recipient's before transfusion	30·0	..	..
		,, ½ hour after transfusion	54·0	..	..
		,, 48 hours ,, ,,	33·0	..	500,000
4	8	Donor's	140·0	..	..
		Recipient's before transfusion	33·0	..	50,000
		,, ½ hour after transfusion	72·0	..	850,000
		,, 24 hours ,, ,,	36·0	..	670,000
5	8	Donor's	146·0	..	..
		Recipient's before transfusion	24·0	2·5	4000
		,, ½ hour after transfusion	46·0	4·0	270,000
		,, 24 hours ,, ,,	28·0	2·5	310,000
6	8	Donor's	93·0	..	..
		Recipient's before transfusion	26·1	4·0	..
		,, ½ hour after transfusion	46·0	..	..
		,, 24 hours ,, ,,	26·8	6·0	..
7	14	Donor's	112·0	..	..
		Recipient's before transfusion	26·1	..	..
		,, ½ hour after transfusion	54·2	..	..
		,, 24 hours ,, ,,	25·4	..	..
8	14	Donor's	182·0	..	..
		Recipient's before transfusion	32·0	3·0	..
		,, ½ hour after transfusion	48·7	28·0	..
		,, 24 hours ,, ,,	31·3	6·0	..
9	16	Donor's	142·0	..	..
		Recipient's before transfusion	33·0	2·5	14,000
		,, ½ hour after transfusion	44·2	9·5	226,000
		,, 24 hours ,, ,,	33·3	3·0	244,000

Results.—Table IV shows that the sodium content of the erythrocytes of stored blood is several times greater than that of the recipient's cells before transfusion. Immediately after transfusion there is a rapid rise in the level of the sodium of cells in the recipient's circulation (which now contains a proportion of donor's cells), and this is to be expected. But in almost every instance the sodium level has returned within 24 hours to that found in the recipient's cells before transfusion. This can only mean that the transfused cells have been destroyed, or that they have been chemically "reconditioned," with the result that the great excess of sodium is removed and replaced by its equivalent of potassium. Parallel figures in table IV and all the data in table II show that disappearance of sodium is not accompanied by a corresponding fall in the count of donor's cells, and it is therefore necessary to conclude that the rapid return of sodium to normal is due to a process whereby the excess of sodium is removed and replaced by potassium. Since this ionic exchange between donor's transfused cells and recipient's plasma must take place against a steep concentration gradient, it cannot be due to any simple physical process. An actual example will make this clear.

In case 9 cells containing 142 mg. of sodium per 100 c.cm. (62 milliequivalents per litre) are given to a recipient whose plasma sodium will certainly be 300–350 mg. per 100 c.cm. (130–150 m. eq.). Yet in this medium so rich in sodium the sodium of the donor's cells falls by 109 mg. (48 m. eq.) to only 33 mg. per 100 c.cm. (14 m. eq.).

If this fall in sodium were accompanied by a corresponding rise in potassium, potassium in the donor's cells would increase by no less than 48 m. eq., although the plasma in which they are suspended will certainly contain less than 6 m. eq. K. These figures for K are only rough approximations, but it is probable that the gain in K of donor's cells after transfusion is many times greater than the absolute K content of the recipient's plasma in which they are suspended. Since, then, all these changes cannot be explained by simple physical processes, one must presume that they are brought about in a much more complex manner. Possibly the spleen, which is known to produce changes in the surface of erythrocytes (Stephens 1938), may play a part.

SUMMARY

Stored blood survives for considerable periods after transfusion. Red cells stored for less than a week show about 70% of survival 14 days after transfusion. If storage is between 7 and 14 days more than half the transfused red cells are still present in the recipient's circulation 14 days after transfusion. During storage normal cells lose potassium and take up a great excess of sodium. Within twenty-four hours of transfusion the chemistry of stored cells is restored to normal.

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SURVIVAL OF THE TRANSFUSED ERYTHROCYTES OF STORED BLOOD*

BY P. L. MOLLISON, M.B. Camb., M.R.C.P.; AND I. M. YOUNG, B.Sc. Lond.

(*From the South-West London Blood-Supply Depot*)

THE opinion that the erythrocytes of stored blood do not survive long after transfusion has been expressed by many authors. Thus Riddell (1939) considers that because of the increased fragility of the cells of blood that has been stored for more than four days "it is very doubtful whether it would exert any prolonged therapeutic effect." Marriott and Kekwick (1940) sum up available evidence as follows: "Red cells of blood conserved for more than a week by present methods do not last long in the recipient." Again, Edwards and Davie (1940) state that "aged erythrocytes and those in which the fragility has been increased have only a short effective span of life and can therefore have little lasting value." These statements are, perhaps, rather surprising since in 1916 Peyton Rous and Turner concluded from their experiments on rabbits that cells stored up to two weeks function normally after transfusion. This conclusion was reached after studying blood-counts, estimating the excretion of hæmoglobin and bile pigments, and so on.

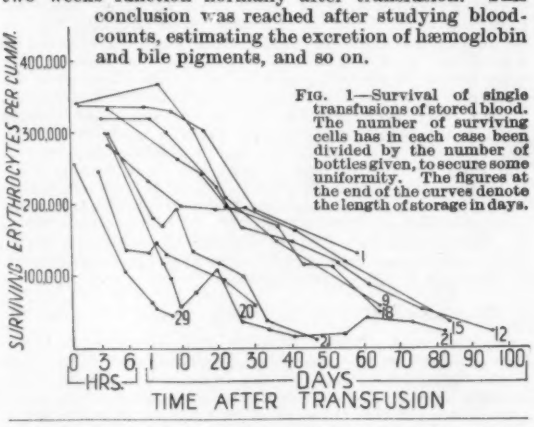

FIG. 1—Survival of single transfusions of stored blood. The number of surviving cells has in each case been divided by the number of bottles given, to secure some uniformity. The figures at the end of the curves denote the length of storage in days.

* The details of this work are to be published later with particulars of technique and methods.

In March of this year we had the opportunity of examining some results obtained by Dr. J. O. Oliver, then director of this depot, and Dr. G. L. Taylor of the Galton Laboratory Serum Unit. They followed seven cases by the direct differential method (referred to below), using M and N agglutinating sera. They showed that transfused erythrocytes of stored blood survived for some weeks after transfusion. In one patient, for instance, who received 11-day-old blood the donor cells could be identified by direct agglutination after 51 days. The object of this investigation has been to extend these observations further and in greater detail and to apply to the problem a method capable of giving quantitative results.

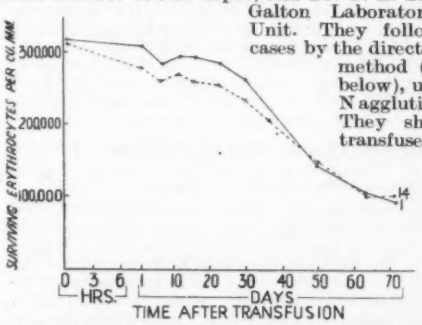

FIG. 2—Survival of two simultaneous transfusions in the same patient. There is scarcely any difference between blood stored for 1 and for 14 days.

Methods of following quantitatively the fate of transfused erythrocytes are all based on the one described by Ashby in 1919. This, in brief, consists of the transfusion of cells of group O to a recipient of group A. After transfusion the recipient's blood contains two types of cells, O and A. The A cells can be "removed" with alpha serum and the free (O) cells counted. Actually a small fraction of the A cells are not agglutinated and constitute a blank value to be deducted from the total of free cells. Wiener (1934) has adopted the method using the sub-groups M and N. For example, if cells of group M are transfused to a recipient of group N, the N cells can be agglutinated and the free (M) cells of the donor counted.

The method of direct differential agglutination consists of transfusing blood containing one of the agglutinogens M or N not possessed by the recipient. This "foreign" agglutinogen is then identified in a sample of the recipient's blood at different intervals after transfusion. We employed both of the quantitative methods and also combined them, either to obtain more certain results with single transfusions, or in order to follow the fate of different transfusions given simultaneously to the same patient. We could thus directly compare the survival of blood stored for short and long periods. This method could also be applied to a direct comparison of methods of storage. A micro-technique was used.

The blood used in these experiments was taken into citrate glucose saline and stored for periods up to 29 days before transfusion. The recipients were mainly women suffering from anæmia connected with pregnancy or parturition.

RESULTS

In fig. 1 the results in a representative sample of the cases are shown graphically. It will be seen that when blood less than 18 days old was transfused the time taken for the complete disappearance of all the donor erythrocytes was 70–90 days—that is to say, little less than that found for fresh blood (Ashby 1919, Martinet 1938). Furthermore, approximately the expected number of erythrocytes appear in the recipient's circulation after transfusion.

In the cases in which a direct comparison between fresh and stored blood was made, similar results were obtained. Fig. 2 depicts one of these cases.

In the cases which received blood over 20 days old a great deal of destruction took place within the few hours after transfusion and considerable rises in serum bilirubin were found.

SUMMARY AND CONCLUSIONS

Twenty-six transfusions of stored blood were given to twenty patients and the survival of the donor's cells was followed quantitatively by differential agglutination.

In four cases two transfusions of blood stored for different periods were given simultaneously to the same patient. The fate of the cells of each transfusion was followed separately by a method employing the sera both of the ABO and MN systems. In this way a direct comparison of the survival of stored blood and fresh blood was made.

A high proportion of the erythrocytes of stored blood survive transfusion. Furthermore, the total time of survival is little less than that of fresh blood.

These observations suggest that the present method of storage employed at the London blood-supply depots is good and that little more than the normal ageing process takes place, at least in blood stored for 18 days or less.

We wish to thank Dr. J. O. Oliver, formerly director of this depot, and Dr. O. M. Solandt, his successor, for advice and criticism; Dr. M. Maizels who provided the impetus for this work and allowed us access to his results at all stages; and Dr. G. L. Taylor of the Galton Laboratory Serum Unit for supplying us with M and N agglutinating sera.

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ASTHMATIC ATTACK STUDIED THROUGH THE BRONCHOSCOPE

BY A. L. D'ABREU, Ch.M.Birm., F.R.C.S.
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I HAVE recently had the opportunity to study the living pathology of an asthmatic attack. The patient was under the care of Prof. G. W. Pickering and Dr. E. I. Jones in the Emergency Medical Service hospital at Harefield, where I was on temporary duty.

Bronchoscopy was carried out to exclude neoplasm in a man of 53, who for the last three years has been suffering from increasing dyspnœa. He has suffered from bronchitis which first affected him in 1917. In the last three years he has become increasingly conscious of shortness of breath associated recently with severe paroxysms at night of an asthmatic nature. His chest is barrel-shaped and emphysematous with scattered moist râles and rhonchi audible throughout the lung fields. The radiological appearances are those of emphysema.

On arriving in the theatre the patient was slightly dyspnœic but not in an asthmatic attack. His lips, tongue, palate and fauces were anæsthetised with a cocaine (10%) spray and both pyriform fossæ painted with the same solution, ten minims of which was then injected through the cricothyroid membrane. The bronchoscope passed easily through the glottis and beyond the vocal cords. I noticed at once that the carina was thicker and redder than usual and as I announced this I saw that it suddenly altered its shape and became "buckled" from before backwards while its covering mucous membrane became crimson. The right and left bronchial orifices contracted to less than their normal size and their membrane was deeply congested; an asthmatic attack developed. After waiting for a short time with gradual coaxing of the instrument I was able with difficulty to pass the bronchoscope into the left and then the right bronchus. All the bronchi were much contracted, the bronchus to the right middle lobe being visible as a mere slit. These bronchi varied slightly from time to time but never relaxed to their normal size. In both main bronchi small fibrin plugs (Curschman's spirals) were seen adhering to the reddened bronchial mucosa. Very little mucus was observed. After removal of the bronchoscope the patient continued in a typical attack of asthma which was not notably relieved by an injection of adrenaline.

The direct observation of these phenomena confirms that the mechanism of the asthmatic attack is bronchial spasm and congestion of the thickened mucous membrane associated with the formation of fibrin plugs. The change in the shape of the carina by a spastic shortening is of interest. I do not know whether this has been noted before.

I am indebted to Dr. K. R. Stokes, deputy medical superintendent at Harefield, for permission to publish this note, and to Professor Pickering and Dr. Jones for their help and interest.

Reviews of Books

Chemotherapy and Serum Therapy of Pneumonia

By F. T. LORD, M.D., clinical professor of medicine, emeritus, Harvard Medical School; E. S. ROBINSON, M.D., Ph.D., director, division of biologic laboratories, Massachusetts Department of Public Health; and R. HEFFRON, M.D., medical associate, the Commonwealth Fund. London: Humphrey Milford, Oxford University Press. Pp. 174. 6*s*.

WITH the approach of the pneumonia season this is a handbook which every interested physician ought to buy and study. The title of the book—the third in a series first published as Lobar Pneumonia and Serum Therapy and then as Pneumonia and Serum Therapy when the range of therapeutic sera was extended to the pneumococcus types which cause bronchopneumonia—indicates the latest advance in the treatment of the pneumonias. It is a compact store-house of useful information on all aspects of pneumonia, and has the advantage over its predecessors of containing data and analyses from Heffron's fine work on pneumonia published in 1939 (see *Lancet*, 1940, **1**, 551). Sulphapyridine was not given a very good reception in America, so that the considered statement of the authors that it is "not only a most useful remedy but also one which is on the whole more efficacious than serum" is praise indeed. The dosage and action of the drug and the results obtained are carefully considered and analysed. Perhaps too much emphasis is given to its possible toxic effects; for example, the authors recommend complete blood-examinations before treatment is begun and each day thereafter, and they disadvise continuance of the drug beyond the fourth day unless the blood-concentration is being estimated daily. Results from therapeutic rabbit antiserum are contrasted with those obtained with horse serum (combined figures show little difference between the two) the relative merits of and indications for serum or chemotherapy are discussed, and a plea is made for combined treatment under such circumstances as when the patient is first seen late in the disease, is over 50 years of age, has a positive blood-culture, is pregnant or does not improve with one or other treatment alone.

Rose & Carless's Manual of Surgery

(16th ed.) By CECIL P. G. WAKELEY, F.R.C.S., and JOHN B. HUNTER, F.R.C.S. London: Baillière, Tindall and Cox. Pp. 1708. 2 vols. 30*s*.

THE successive authors of this excellent textbook have had the happy knack of giving the undergraduate exactly what he wants. This has necessitated considerable changes which are particularly notable in the present edition. The first eight chapters on general pathology have been simplified and shortened; a very welcome revision. Simplification and clarification have also been obtained by combining the chapters on shock and hæmorrhage and those on gangrene and ulceration. A section on the treatment of war wounds has also been added. There have been so many advances or alterations in the management of fractures, diseases of the central nervous system and chest conditions that extensive revision had to be carried out, and no less than 300 illustrations appear in the text for the first time. The scope of the book is wide enough to supply the practitioner with a trustworthy guide to all branches of surgery.

Biochemistry of Disease

By MEYER BODANSKY, Ph.D., M.D., director of the John Sealy memorial laboratory and professor of pathological chemistry, University of Texas school of medicine; and OSCAR BODANSKY, Ph.D., M.D., lecturer in biochemistry, graduate division, Brooklyn College. London: Macmillan and Co. Pp. 684. 30*s*.

THIS book embraces the whole field of clinical biochemistry. Several such textbooks already exist, but the unusual presentation of the Bodanskys' work gives it an exceptional value. General presentation of carbohydrate, fat, protein and mineral metabolism, and descriptions of chemical methods are avoided. The subject matter is arranged according to clinical entities, and thus there is a systematic presentation of the biochemical aspects of the various diseases. A mass of biochemical information is in this way made readily available to clinicians who do not require to read through technical methods before obtaining the necessary information. Useful information is given on prothrombin and vitamin K, diseases of the endocrine glands, and on the neglected subjects of biochemistry in obstetrics and gynæcology and the biochemical aspects of neurological and psychiatric disorders. Each chapter contains a full list of references. Practitioners, students and clinicians will find the book of outstanding value for reference and as a review of recent work.

Pharmacology and Therapeutics of the Materia Medica

(16th ed.) By WALTER J. DILLING, M.B. London: Cassell and Co. Pp. 580. 12*s*.

THE recent alteration in format has made this useful manual much more readable. In a book of this type it is not possible to deal exhaustively with many subjects, but more than two pages might have been spared for the sulphonamide compounds. The new preparations of vitamins A and D which became official in June, 1940, with the publication of the Second Addendum to the British Pharmacopœia 1932 are included, and an indication of the international upheaval is seen in the official pharmacopœial names now adopted for drugs previously known under trade names.

Handbook of Radiography

By JOHN A. ROSS, M.A. Camb., M.R.C.S., D.M.R.E., radiologist to the Warrington Infirmary. London: H. K. Lewis and Co. Pp. 126. 7*s*. 6*d*.

A HANDBOOK for medical technicians must always be dogmatic if it is to avoid confusion. For this reason a textbook intended for the student pharmacist is of little value to the student of pharmacology. The same applies to the radiologist and the radiographer—on the one hand the training is scientific, on the other technical. Dr. Ross writes for students of both radiology and radiography, and therein lies a weakness. However, as he points out, there is undoubtedly a place for a handbook on radiography like this, illustrated with simple line drawings. The book has the advantage of being easily portable, and blank pages for notes are an excellent idea. Some form of tabulation for each technique would be useful, giving specific figures for such factors as kV, mA, time, distance, size of diaphragm or cone, size of film, screens, grid, angulation of tube, position of central ray, method of immobilisation of part, and stereoscopy. The radiographer could then modify each factor according to the requirements of each individual apparatus and radiologist and enter them up on the opposite blank page. Sufficient stress is not laid on the necessity for taking at least two right-angled views in most branches of radiography. For example, only one projection is described for the shoulder. Here stereoscopy is recommended, but it will never be a satisfactory substitute for another view at right angles. Stereoscopy should always be regarded as an ancillary method of examination. In the chapter on the skull the special projections, such as are required for the petrous bone, are scarcely mentioned, and these are some of the most difficult views that a radiographer is called on to produce. There are one or two other omissions, such as arthrography and the outlining of the pancreas by filling the stomach with gas, but otherwise the radiographic field is well covered.

Principles of Animal Biology

(2nd ed.) By LANCELOT HOGBEN, F.R.S. London: George Allen and Unwin. Pp. 415. 7*s*. 6*d*.

WHEN first published in 1930 Professor Hogben's book was an innovation, and probably for that reason never became popular with teachers. While insisting on the need for a knowledge of sound established facts, and giving many useful hints as to how they can be learnt, his chief aim is to give the student an insight into the biological problems of today. In the successful combination of these two aims this book is unsurpassed. It would be difficult to find a better elementary introduction to modern genetics than chapter VIII, with its admirable series of problems to be solved. The new edition has been extensively revised and has been illustrated afresh by J. F. Horrabin. Professor Hogben's reputation has increased since 1930, and it is certain that this edition will enjoy a much wider circulation, which we hope will include members of the schools and universities.

THE LANCET

LONDON: SATURDAY, OCTOBER 5, 1940

CASUALTIES IN LONDON

Now that the Philistines are upon us we can judge the quality of our own foresight. With air-raid casualties, as with any other wounded people, the aim must be to ensure that urgent cases are treated first. Early expert classification would make this possible, but it cannot be achieved in the peace-time hospitals of London; they are not laid out for it, they are dangerous, and they are in the wrong places. Their vulnerability has been amply demonstrated lately, and it was not unforeseen. We drew attention to it in an annotation last year,[1] and in the same issue CROME, FISHER and SHIRLAW [2] advocated casualty clearing stations in the basements of steel-framed buildings—buildings to be chosen not for their traditional associations with healing but because they were safe, and close to main lines, underground railways or arterial roads by which patients fit for transport could be evacuated. They pointed out that the London hospitals, besides being old and collapsible and badly placed for transport, were so well known in their own neighbourhoods that in any large disaster they would be overwhelmed by patients hurrying to an accustomed refuge. They also urged the vital importance of skilled classification, which cannot be left to first-aid workers, however willing. These can, as they said, divide patients roughly into "those who can be sent home, to the surgeon or to the mortuary," but they are totally unqualified to say which need priority of treatment or which are able to support a journey out of London by train or ambulance. That is a task for an experienced surgeon; it calls for concentration and cannot be carried out with precision in premises in the front line shaking under the impact of neighbouring explosions. Moreover, some of the patients need immediate operation to save their lives or limbs, and the operating surgeon can do his best for them only if he is protected while he works.

Fortunately we are told that casualties in London have so far been fewer than the authorities expected, but that hardly excuses the inadequacy of existing arrangements, especially since an effective alternative can be put into action with little trouble or cost. In every dangerous area it would be possible, as SHIRLAW says in his book,[3] to set aside for the reception of casualties a capacious basement—there are many available among the steel-framed factories, warehouses, garages, hotels and office blocks of London—close to a railway or main road or both. This would be subdivided into four departments. In one the patients would be at once classified by the receiving surgeon as suitable to be sent home, transferred by ambulance or train to an outlying hospital in the sector, operated on without delay, or given restorative treatment to fit them for operation in an hour or two. Those suitable for transfer would be taken at once to the evacuating department and sent off. Those requiring restorative measures would be taken to the resuscitation department to be put to bed by the nursing staff. Cases for operation would go to the fourth department and receive the care their injuries required. Where a single basement of sufficient size was not available the various departments would be in separate buildings, as close to each other as possible. Gravely injured patients would receive treatment according to their needs, surgeons and nurses would work protected from anything short of a direct hit, and cases for transfer would be sent off quickly enough to avoid congestion. A large number of beds would not be required, but those that there were would be placed in sufficient safety to give patients the sense of security for which they crave.

SHIRLAW gives the name classification evacuation points (C.E.P.) to these centres. His plan is doubtless imperfect, as all improvised plans must be, but it has obvious advantages over the existing system. The bombardment of London may last a long time and if we have put off making proper provision before the event nothing justifies delay now that we know what to expect.

1. *Lancet*, 1939, 1, 650.
2. Crome, L., Fisher, R. E. W. and Shirlaw, G. B. *Ibid*, p. 655.
3. Casualty Training and Organisation, London, 1940; see *Lancet* Aug. 24, 1940, p. 231.

CHRONIC MASTITIS

THE dependence of mammary growth and function on hormones has been amply demonstrated by experiment. The gonadal hormones, and artificial compounds with similar biological properties, are readily available and by their means the physiological activities of the mamma can be largely controlled. Clinicians have hoped, not unreasonably, that some of the pathological activities might be controlled by the same means. Changes closely resembling those of chronic mastitis in women can be produced in animals by œstrogens.[1] In women the exacerbation of pain and lumpiness in the mamma about the time of ovulation—that is to say when the output of œstrogen is at a maximum—leaves little doubt, when considered with knowledge derived from experiments on animals, that so-called chronic mastitis in women is attributable to a relative excess of œstrogen. One method of diminishing the output of œstrogen by the ovary is to supply testosterone, which reduces the output of gonadotrophin from the pituitary. Unfortunately androgens given in amounts sufficient to relieve mammary discomfort may have other effects which are undesirable.

On another page ATKINS gives in detail the results of treating 34 patients with testosterone propionate given by injection in doses usually exceeding 400 mg. during four weeks. Among these 34 patients 25 were benefited by the treatment so far as the breast condition was concerned, but hairiness, amenorrhœa and deepening of the voice were noted in 8 and menstruation was upset in others. In the goat and rabbit œstrogens have been found to be most effective when applied directly to the mamma.[2] MACBRYDE [3]

1. Goormaghtigh, N. and Amerlinck, A. *Bull. Cancer*, 1930, 19, 527; Lacassagne, A. *C.R. Acad. Sci. Paris*, 1932, 195, 630; Burrows, H. *Brit. J. Surg.* 1935, 23, 191.
2. de Fremery, P. *J. Physiol.* 1936, 87, 50 P. Lyons, W. R. and Sako, Y. *Proc. Soc. exp. Biol.* 1940, 47, 398.
3. MacBryde, C. M. *J. Amer. med. Ass.* 1939, 112, 1045.

made a similar observation in women. SPENCE [4] has used this knowledge in his treatment of women with chronic mastitis. To eliminate psychological effects he first gave his patients, unknown to them, an inert ointment which they used for a month. The symptoms continued under this treatment and an ointment containing testosterone or its propionate was then substituted, a regulated amount being rubbed into the mamma every night. The doses of hormone so used ranged from 4 to 10 mg. a day, thus being considerably less than would be effective if given by injection. The 8 women treated in this way were all relieved of mammary pain, and none of them developed hairiness or amenorrhœa. Œstrogens appear to affect the mamma indirectly through their action on the pituitary. In spite of this fact there is experimental evidence that their action on the mamma is greatest when they are applied locally. From SPENCE's observations it would appear that the same is true of testosterone. Oddly enough, in view of what is known of the causation of chronic mastitis, beneficial results have been claimed for its treatment with œstrogen, but of the 33 cases treated by ATKINS with œstradiol benzoate or stilbœstrol 15 were rendered worse, amelioration was claimed by only 4, and 14 were unchanged. These results are in accord with expectations based on experimental knowledge.

The new work affords valuable guidance in the treatment of a condition which has been distressing to both patients and their doctors, for it shows a definite prospect of combating the symptoms by testosterone. A useful step now would be to improve the nomenclature. The machinery of the mind is impeded every time one is compelled by custom to apply the term mastitis to breast changes which we know are not mastitis. The pathology being now known, there is every reason for adopting the term "œstrogenic mastopathy" or some more euphonious version of it.

M.R.C. MEMO ON GAS GANGRENE

THE War Wounds Committee of the Medical Research Council have done a good job of work in publishing a concise account [5] of what gas gangrene is, and the methods by which it can best be prevented and treated, for few of the younger surgeons have much first-hand experience of this dreadful infection. The memorandum rightly emphasises that gas gangrene, principally an infection of muscle, is a clinical conception, so that the diagnosis must be made at the bedside and not in the laboratory. The spore-bearing anaerobes of the gas-gangrene group are often present in wounds where there is no gas gangrene, and as in diphtheria the clinician must learn to act on signs and symptoms and not wait for the bacteriologist's report. The acute onset and rapid progress are a feature of the infection, so that cases may be in extremis within a few hours of wounding, although as a rule the infection develops in wounded men who have been left unattended for 24 hours or more. The committee discuss the signs and symptoms, the quickening pulse, the local pain, the anxious look, the swollen limb with signs of gas-formation, and they warn the reader against relying on skin changes, which are variable, usually late and no indication of the extent of infected muscle, and point out the fallacy of X-ray diagnosis. If gas gangrene is a clinical conception it also depends for its occurrence—and this point is insufficiently made in the memorandum—on a combination of suitable conditions. It requires gross damage of tissues, having a high association with bony fracture, and a soil rich in the sporing anaerobes, but the most important single exciting factor is delayed surgical attention. The last fact is well illustrated by an American experience [6] in the 1914–18 war. Among 349 severely wounded and therefore non-transportable men who were operated on within 24 hours of injury there was no case of gas gangrene, whereas infection developed in 5% of some 4000 wounded men sent to an evacuation hospital with an average interval of 41·8 hours between injury and operation. For this reason, if for no other, it is supremely important to arrange for early surgical attention to air-raid casualties. That does not mean that a few hospitals in the near vicinity of the raided districts should be overcrowded, or that the injured should be evacuated wholesale to base hospitals, but rather that casualties should be dispersed in small numbers to as many hospitals as are within easy reach. The Spanish war demonstrated the wisdom of this policy.

The memorandum deals briefly with surgical prophylaxis and treatment, advocating ruthless excision of infected muscles but perhaps wisely avoiding any reference to the best method of amputation. As regards medical measures it recommends both the sulphonamides and antitoxin, particularly for treatment of the established case. Information is needed about the usefulness of the sulphonamides as prophylactics per se; possibly they act mainly by attacking concomitant aerobes which predispose to anaerobic infection. For treatment dosage by mouth is advised, but surely with the patient in a shocked state with absorption from the gut unreliable and the further risk of gastric upset, it is more rational to give the drug intravenously, if necessary in plasma or whole blood, or locally into the wound after surgical excision. Incidentally, either sulphanilamide or sulphapyridine is recommended, although experimental evidence suggests that the latter drug is much the more efficacious.

The memorandum concludes with a suggested scheme drawn up by the London sector pathologists for the bacteriological investigation of war wounds, with a brief discussion of the collection of specimens and the methods for identification of the common pathogenic bacteria in war wounds—streptococci, staphylococci and the gas-gangrene anaerobes. Litmus milk is recommended for the detection of *Clostridium welchii* although its activity as a gas-producer can be as readily detected in Robertson's meat broth. Why the objection to the screw-cap bottle for this medium? The identification of the anaerobes is the main difficulty, and unfortunately the table given will not help much. *Cl. welchii* apart, the recognition of the spore-bearing anaerobes by morphology and colonial appearance is a hard task, and it would be more useful to devise a scheme

4. Spence, A. W. *Lancet*, Sept. 28, 1940, p. 387.
5. Notes on the Diagnosis and Treatment of Gas Gangrene. M.R.C. War Memo. No. 2. 1940. H.M. Stationery Office. 3d.
6. United States History of the World War. Medical Department of the U.S. Army in the World War. Washington, 1929, vol. xii, p. 413.

for the early identification of these pathogens by toxin-production and animal-pathogenicity tests. But everyone will agree with the committee on the need for keeping careful records which will provide more precise information about war-wound infections, supplement clinical data on the effect of various treatments, and secure evidence about hospital cross-infection.

SYNTHESIS OF A DISEASE

IN 1869 JONATHAN HUTCHINSON described some curious skin lesions on the fingers, forearm and shins of a man. They were painless raised dark purple patches apparently formed by the confluence of discrete "tubercles"; they were irregular in their margins, smooth or finely scaly on their surfaces, and could be flattened by prolonged pressure. In 1889 BESNIER described this condition in greater detail and christened it lupus pernio. In 1898 HUTCHINSON published illustrations of a somewhat similar condition in which persistent raised dusky-red patches appeared in almost symmetrical groups on the two sides of the body. Ten years later BOECK of Christiania described this second condition more fully, clinically and histologically, under the name "multiple benign sarcoids of the skin"; he traced their evolution over a period of years, found analogous lesions in various mucous membranes, and noted that they might be accompanied by glandular enlargement. In 1914 SCHAUMANN of Stockholm showed that lupus pernio and multiple benign sarcoids have the same microscopic structure, and moreover that they are only two manifestations of an affection which may involve many of the viscera as well as the lymph-glands.

The new-formed tissue of the disease is the same in whatever site it develops. It consists of accumulations of epithelioid cells, interspersed with some lymphocytes and a few large giant cells, whose numerous nuclei are scattered throughout their cytoplasm; it fibroses as it grows old but it never caseates. It differs therefore from the tubercles which are evoked by the presence of the tubercle bacillus, and the long controversy about the tuberculous ætiology of the various lesions of this disease is now pretty well at an end. The disease is looked on as a peculiar reaction of the reticulo-endothelial system to an unknown stimulus. The disease affects the eye, producing the appearance of an iridocyclitis, which is often without further inquiry labelled tuberculous. Such an iridocyclitis, associated with fever and swelling of the parotids, was named "uveoparotid fever" by HEERFORDT in 1909; facial palsy may be incidental to it. Among the lymph-glands, any of which may be involved, with or without the spleen, the commonest site for the condition is the mediastinal group; their enlargement is apt to be regarded as tuberculous, if not even lymphadenomatous. In the lung sarcoids can occur, in large numbers and widely disseminated; they cast shadows that may easily be mistaken for those of miliary tuberculous lesions, though they are a little coarser, and they may cause breathlessness and cough. From the reticulo-endothelial tissue of bone-marrow sarcoids may grow, commonly in hands and feet; they cause bluish-red spindle-shaped swellings of digits, which resemble the truly tuberculous "spina ventosa," but on radiography show the punched-out areas in the phalanges called by JÜNGLING "osteitis tuberculosa multiplex cystica." In autopsies lesions have also been found in spleen, liver, intestine, testicle, brain, tonsils, and heart.

The disease may have an acute phase, with fever and increase of the red-cell sedimentation-rate, but mostly runs a very chronic course, tending after years toward spontaneous recovery. No treatment cures it. There have been several reviews of it published in the last few years, of which the most recent is by Prof. C. G. LAMBIE[1] of Sydney; he reports several cases of his own and cites an extensive bibliography. Professor SNAPPER's lecture on it, given in London in 1937, has been published as a beautifully illustrated monograph.[2] The history of the condition is interesting, because its various manifestations, first described as distinct diseases, have been amalgamated into one "entity"—a simplification as welcome as it is rare in medicine. Its diagnosis is a pitfall to the one-track specialist; it may be missed by the dermatologist or the chest physician who ignores the eyes, by the ophthalmologist who does not inspect the skin or palpate the glands and the spleen, and by the radiologist who looks no further than his films. Yet its recognition is important, for it is commoner than is widely realised, and its prognosis is almost always better than that of the tuberculous lesions with which it is easily confused. Its troublesome aspect, at present, is nomenclature. Boeck's sarcoids or sarcoidosis is a common name for it. The Besnier-Boeck disease has official sanction from a dermatological congress. Professor LAMBIE recommends Besnier-Boeck-Schaumann syndrome (which seems hard on Jonathan Hutchinson), but he rightly points out that it will require the discovery of its cause, not merely its synthesis on histological grounds, to provide it with a satisfactory name.

BULLETIN OF WAR MEDICINE

IN the last war the Medical Research Council (then Committee) brought out a monthly medical supplement to the Daily Review of the Foreign Press issued by the War Office. This supplement first appeared in 1918 and contained abstracts and summaries of foreign medical work. The council has now published the first number of a new *Bulletin of War Medicine*,[3] which differs from its predecessor in containing a survey of work done in this country as well as abroad. Fortunately for mankind medical science has no frontiers and the new journal is a reminder that throughout the world men share an enthusiasm for building up as well as breaking down. The abstractors are experts in the subjects they summarise which cover all branches of the science of medicine that may apply to war conditions. This number has sections on wounds and injuries, surgery of special regions, plastic surgery, anæsthesia, blood-transfusion, X rays, general and special diseases, psychological medicine, war gases and explosives, pharmocology, naval and aviation medicine, industrial hygiene, and food and drink, sanitation and civil evacuation. The bulletin does not cover tropical diseases or public health which already have their own bulletins. British, Dominion, American, German and French journals are passed in review and only rarely is the survey too general to be informative. It will be a great achievement to maintain this standard at bi-monthly intervals.

1. *Med. J. Aust.* 1940, 1, 815.
2. Snapper, I. and Pompen, A. W. M. Pseudo-tuberculosis in Man. Part 1. Haarlem. 1938.
3. Edited by the staff of the Bureau of Hygiene and Tropical Medicine under the direction of H. Harold Scott, M.D., F.R.S.E. H.M. Stationery Office. 2s. 6d.

Annotations

TREATMENT OF BLAST CONTUSION OF THE LUNG

OCCASIONAL examples of contusion of the lung by high-explosive blast are probably being admitted to casualty hospitals, though no further cases have yet been reported since those of Allison and his colleagues,[1] and where they are diagnosed there will be some doubt as to the right treatment. All of them will be suffering from shock and most from severe burns, fractures or other injuries, and the chest condition will have to be borne in mind when planning the repair of other parts. In resuscitation it must be remembered that bleeding has been taking place from the capillaries of the pulmonary artery lying relatively unprotected in the walls of the alveoli, and if it has stopped it may easily start again. There is a danger that transfusion, whether with whole blood, plasma or glucose-saline, may add to the risks by promoting œdema of the lung bases. There seems to be good reason, therefore, for withholding transfusion, at least in the early stages, and combating shock by other methods, of which those which stimulate the peripheral circulation are probably the safest. Experience with bilateral pneumothorax treatment in tuberculosis has shown that a patient at rest in bed can get along quite comfortably with a very small area of functioning lung tissue, so that unless the contused area is extensive active measures of resuscitation are not needed from the point of view of opening up the lung parenchyma, though they may sometimes be necessary for cardiac stimulation. Continuous oxygen administration should have its place, more particularly if cyanosis is present. Posture is important. Blood from the contused area should be prevented from trickling down bronchi into the unaffected lung. The hæmorrhage, unlike that of pulmonary tuberculosis, usually affects the bases, and the best position for the patient is with the shoulders raised. If the bruising is unilateral he should be placed with the contused lung downwards, to prevent aspiration into the sound side. The use of morphia, so long an established practice in hæmorrhage, must here be approached with caution, and certainly the heroic half-grain doses given for hæmorrhage elsewhere are unwise. The deciding factor is the patient's mental condition, and a small dose to allay restlessness—not more than gr. ¼, repeated if necessary—is all that is required. There is clinical evidence that adrenaline is not free from danger where œdema of the lung is to be feared, and yet it might help to overcome temporary spasm of the bronchioles. Atropine to diminish exudation seems unobjectionable. Where an anæsthetic is essential it should be a local one or Pentothal.

The general principles of management, then, are the same as in bronchopneumonia, with additional precautions against hæmorrhage. Little is yet known about the later results of a contused lung in those who survive the initial shock. Secondary infection may follow, producing a condition clinically resembling postoperative pneumonia. Whether the affected base will ever function normally again is doubtful.

TIC DOULOUREUX TREATED BY DIATHERMY

THE usual treatment of trigeminal neuralgia, when the pain cannot be controlled by analgesics, is alcohol injection of the offending division of the nerve or of the gasserian ganglion itself. The success of this operation depends on skill, which only comes from much experience with the condition, and a detailed knowledge of the anatomy of the basis cranii and even in the best hands the results may be uncertain. Neurosurgeons have therefore devised alternative methods; open operation enables nerve section to be performed with certainty, and excision of the ganglion through a lateral approach to the middle fossa has become one of the more usual operations. If they are to be successful these methods must produce complete anæsthesia of the area. When the third division of the trigeminal nerve alone is cut little disability results, but when the ganglion itself is destroyed there is anæsthesia of the face, cornea and tongue, and sometimes the motor division is destroyed as well. The ungrateful patient then complains of the discomfort, suppressing memories of the excruciating agonies from which he has been freed. Moreover, such complications as ulceration of the anæsthetic cornea or a peculiar continuous pain sometimes follow alcohol injection. The subject has been closely studied by Harris.[1] To obviate these disadvantages Sjöqvist[2] devised an operation to cut the spinal tract of the trigeminal nerve within the medulla. This results in loss of pain and thermal sensation in the affected side of the face, with absolute preservation of the other forms of sensation, and is not associated with the risk of corneal ulceration. Obviously the task of cutting a tract in the medulla, however superficial, is not to be undertaken lightly, and the heroic procedure has been appropriately referred to as a young man's operation.

Eybers[3] claims that electrocautery of the ganglion produces more certain relief from pain with less undesirable sequelæ than alcohol injection. The procedure is similar to that used in injection, but the needle, except for its tip, is insulated in vulcanite. It is introduced into the ganglion by way of the foramen ovale, the anterior approach being as a rule the most favourable. An indifferent electrode is placed elsewhere on the patient and a small coagulating current is passed to the needle tip for twenty seconds. The cauterisation is repeated, and it causes degeneration of the ganglion cells with resulting relief from the pain. Eybers says that this relief is not associated with such profound sensory loss as with the other procedures. Unfortunately most authorities would agree that where any sensation remains the pain is liable to return within a few weeks or months. The method has been practised on the Continent in the last few years, especially by Kischner in Heidelberg, and although it is open to many of the disadvantages of injection it seems to be more certain and more readily controlled. Since their technique is so much alike the two procedures can be readily compared, and a follow-up will soon show which is the one of choice.

RECOVERY AFTER CEREBRAL COMPRESSION

MANY surgeons have had the disappointing experience of a patient failing to recover after the successful evacuation of a large intracranial hæmatoma. The brain sometimes fails to expand after the clot has been removed, and two such cases, both extradural hæmatomas, led Reid[4] to a study of the factors concerned in the expansion of the brain after the relief of compression. From a series of observations on cats he concludes that the most important physical factors are the degree of compression, the rate at which it has developed, and the length of time it has acted. As an important secondary effect, the return of fluid displaced from the cellular elements and the intercellular spaces plays a considerable part in the recovery of the normal bulk and contour of the brain. The brain will expand most quickly and completely when it has been compressed for a short time by a rapidly developing lesion which has not attained large size and has not displaced much fluid from the cells and tissue spaces. These are satisfactory explanations of delayed or incomplete expansion, but this may be only one of several factors which play a part in the fatal cases. In addition to the obvious compression by a large clot, and the failure of the brain to expand after the clot is

1. Dean, D. M., Thomas, A. R. and Allison, R. S. *Lancet*, Aug 24, 1940, p. 224.

1. Harris, W. The Facial Neuralgias, London. 1937.
2. Sjöqvist, O. *Acta Chir. Scand.* 1939, 82, 201.
3. Eybers, von W. *S. Afr. med. J.* Aug. 24, 1940, p. 324.
4. Reid, W. L. *Med. J. Aust.* 1940, 1, 885.

removed, there may be the more subtle effects of the injury on neurones—effects which defy present pathological technique. There are fatal head injuries in which from naked eye and microscopic examination it may be impossible to say why the patient died. Nevertheless, the explanation of known facts will help to simplify the problem. Reid's conclusions argue for the relief of cerebral compression at the earliest possible moment, and if any additional evidence was necessary most surgeons could cite experiences of how rapidly a patient with an extradural or subdural hæmatoma can die even under observation in hospital, before facilities for operating can be mobilised. Diagnosis remains difficult, and too often the uncertainty arises from the lack of a thorough examination as soon as possible after the injury. Only by such an examination can a base-line be established on which to assess the signs of progressive cerebral compression.

SILK OR CATGUT

THE rival claims of suture materials are still unsettled and a surgeon's preference for silk or catgut often rests on a personal whim. Silk has the great advantage that it can be perfectly sterilised, but the great disadvantage that it remains a permanent foreign body in the tissues. Catgut cannot be sterilised by heat without losing its tensile qualities, and the chemical processes of sterilisation are not always perfectly reliable; nor is catgut so easily absorbed that it is not sometimes extruded as a foreign body, especially in the presence of infection. Nevertheless most surgeons nowadays prefer catgut. Daniel C. Elkin[1] is not one of these, and in a five-year study of wound infection at the Grady Hospital, Atlanta, Georgia, he finds evidence to support his preference for silk. All operation cases were classified as clean, potentially infected, or infected; the progress of healing of the wounds was carefully watched, and the development of the slightest signs of infection noted. Emergency operations done by the resident staff constituted the majority of cases. Silk was used in approximately two-thirds of the clean cases and 2·1% of these became infected. Catgut was used in the remaining third and 9·4% of these became infected. Catgut was used in the majority of potentially infected cases (such as compound fractures, wounds, and gangrenous appendicitis) and the number of these becoming infected was nearly three times as many as of those in which silk was used. On the face of it such evidence is fairly convincing, but the problem is not so simple as these few figures might make it appear. No-one would contend that the use of a particular suture material was the only or even the main factor in postoperative wound infection: Elkin himself mentions many of the other important factors when he describes Halsted's technique "based upon complete hæmostasis, clean dissection, the avoidance of mass ligatures, undue tension, and meticulous attention to every detail which eliminated tissue trauma," and he admits that his five-year inquiry "led to better care of the wound throughout the operative procedure." In these circumstances it is surely unjustifiable to give all the credit to the suture material even though silk came to replace catgut in the majority of operations. During one year the incidence of infection in "clean" cases was almost the same whether catgut or silk was used. This was because of the high proportion of infections among patients of one operator—a significant comment on the difficulty of interpreting statistics. These figures, however, even if they do not prove that silk is superior to catgut in allowing smooth healing of wounds, do at least show that given a careful technique silk may safely be used in contaminated wounds. In a discussion of Elkin's paper opinions were on the whole in favour of catgut. One surgeon, after using first catgut and then silk in thyroid operations, had finally returned to catgut. Another said "I took 100 cases and used silk, and a second 100 cases and used catgut, and in my hands catgut was far superior to silk," but he summed up the situation later by remarking "'Every one to his own liking,' said the old lady when she kissed the cow."

1. *Ann. Surg.* August, 1940, p. 280.

AN AZTEC HERBAL

ELEVEN years ago Prof. C. U. Clark, with his remarkable flair for discovering unique manuscripts, found in the Vatican library an Aztec herbal which, on the authority of Prof. H. E. Sigerist, who contributes a foreword to the translation,[1] is America's earliest medical work. The date is 1552, that is to say only thirty years after the Spanish conquest and almost contemporary with the famous European herbal of Dodonæus and a decade later than those of Fuchs and Gesner. The coloured illustrations of the Aztec herbal, though somewhat conventionalised and rather in the style of the Ortus sanitatis, represent 184 native plants and materially assist in the task of botanical identification, and fortunately the generosity of the Smithsonian Institution and other bodies, as well as of private individuals, has made it possible to embody a complete facsimile reproduction in colour of the manuscript with the translation. The manuscript was written by an Indian teacher of medicine, Martinus de la Cruz, in Aztec and translated by another Indian, Juannes Badianus, into Latin. Miss Emmart makes it clear that, unlike later works, the Badianus text represents Aztec medicine unmodified by European interpretation. The remedies, like those of contemporary European practice, were usually a mixture of many ingredients, on the principle that if one fails another may succeed. A good example is the remedy for "the fatigue of those administering the government and holding public office." This is composed of the bark of a tree, the leaves of twelve others, the flowers of eight plants, besides fruiting almond. To this was added the wood of hæmatoxylin, the blood of eight different animals, five kinds of precious stones, white clay, the bezoars from three different birds, also the brain and bile of seven other animals. Such a list of forty-seven ingredients rivals the receipts in the Saxon Leechbook of Bald. Some of the remedies were clearly in the nature of charms, and a belief in a "doctrine of signatures" is suggested by the use of hairy caterpillars as an ingredient in the remedy for falling hair. This doctrine was sincerely believed by many in Europe and led to the careful examination and observation of plants which laid the foundations of taxonomic botany, just as the search for the philosophers' stone and the belief in the transmutation of elements helped materially to advance the knowledge of primitive chemistry. Despite the superstition which was then characteristic of medical lore the world over, the Aztecs were fully aware of the value of the daturas as narcotics and used bocconia as an analgesic. *Ipomega purga,* one of the "jalaps," was used as a purgative, as at the present day, as also was *Cassia grandis.* Hæmorrhoids were treated by means of purgatives, intermittent fevers were recognised and their treatment, which included emetics, antipyretics and stimulants, was adapted to the course of the malady. The treatment of earache was a combination of astringent washes applied within, and external applications of datura. The pharmaceutical and botanical interest of this early manuscript is considerable, but despite the researches of Miss Emmart into later works and such assistance as the illustrations afford it has only been possible to identify with any certainty about a quarter of those figured although more than half can be tentatively identified. Now that the text is available further botanical research

1. The Badianus Manuscript. Introduction, translation and annotations by Emily W. Emmart. London: Humphrey Milford, Oxford University Press. Pp. 341. 53*s.* 6*d.*

in Mexico will no doubt diminish the unidentified residue. Among the more interesting of the plants mentioned the root of smilax (sarsaparilla) appears in a remedy for scabies. Of the definitely recognisable figures that of *Theobroma cacao* is the earliest known illustration of the cocoa tree. Most of the plants are unfamiliar but some are even found as natives of the Old World—for example, reed mace and milfoil—while not a few are cultivated garden plants, among them the red-flowered dahlia, the begonia and commelina.

PREVENTION OF SILICOSIS

SILICOSIS in coal-mines is not the pressing problem in the Netherlands that it is in this country, but Dr. A. H. Vossenaar,[1] chief medical officer of the United Collieries at Limbourg, views the two aspects of control—the condition of the worker and the conditions under which he works—from a long experience. He insists on the need for a preliminary radiographic examination of all underground workers, special importance being attached to the physical condition of those intended for work on rock, which exposes them to a greater risk of contracting silicosis. A re-examination every three years should include radiographic examination and an investigation to ascertain any predisposition to the effects of dust or to intercurrent diseases which would have an unfavourable influence. Vossenaar makes a definite plea for the limitation of the period of dangerous work underground. He puts this at 12–15 years of rock work, after which a change of occupation should be given, and he suggests that this condition should be made known to the worker at the outset so that he would not regard his transfer as meaning that his health was impaired. In discussing the technical procedures for the control of dust at the work places Vossenaar urges the importance of suppression of dust at the point of origin, whether by exhaust or wet methods. He recommends the use of masks when the dust cloud cannot be localised, as after shot-firing; the mask should fulfil the requirements of efficient filtering capacity, low resistance, small "dead-space" and good fit. He advocates good ventilation, improved mechanical loading and transport, wetting of broken rock and limiting of shot-firing to the end of the shifts, and it is now possible to assess the efficacy of such systems of dust suppression by estimating the numbers and size frequency of dust particles in the atmosphere. Finally Vossenaar points out that the general welfare of the worker depends on the provision of good conditions in his home as well as in his working environment, and the maintenance of his standard of living during disablement or unemployment.

Dr. Charles Badham[2] reports from Sydney the result of some investigations into the air-borne dust in tunnels and trenches in the highly siliceous sandstone on which the city stands and through which its system of sewers had to be hewn. In one tunnel, 5 ft. by 3 ft. 6 in., the concentration of dust was from 400 to 10,000 particles per c.cm. (as a rule the workers were exposed to several thousand particles per c.cm.) with a pneumatic pick and water blast in use and with the ventilating exhaust pipe 5 ft. from the face. Badham recommends an axial water-feed pick with improved ventilation and with the exhaust pipe one foot from the face. In a trench 10 ft. deep, working with a pneumatic pick on the hard sandstone floor of the trench, with the water disconnected, the concentration reached over 6000 particles per c.cm. within a few minutes. With water connected the concentration was 1596 particles per c.cm. The limit of safe working aimed at in Sydney is 200 particles per c.cm. at the breathing level of the worker. From the tests made it is evident that to attain even this arbitrary standard the utmost care is required in selecting the type of tool for the purpose, and in providing and maintaining correct and adequate ventilation. This means continued investigation at the actual working places by scientific methods and the application to each case of the results of the researches.

1. *Med. Off.* August 31, 1940, p. 69.
2. Annual report of the Health Department (division of industrial hygiene) for 1938, Sydney, N.S.W.

EMOTIONAL ADJUSTMENT OF THE DIABETIC CHILD

A COMMON belief that diabetic children are more intelligent than the average is not supported by the studies of McGavin and her colleagues[1] upon 49 children under the age of eighteen. The children were American born, 36 of them of parents born in the United States; the remainder were of mixed heredity, German predominating. The number of children in the families varied from 1 to 10, and it may be noteworthy that 17 of the children were the eldest and 15 the second child in the family, but the authors do not state how many families had only 1 or 2 children. In 8 of the children there was a paternal and in 9 a maternal history of diabetes; in 2 both sides of the family were involved. Of a pair of identical twins only one child was diabetic. The children on the whole were healthy; 2 died during the investigation, and 4 others developed ailments, 6 had physical defects and 2 visual defects.

Their intelligence was assessed by the revised Stanford-Binet scale, Ferguson form boards, the Metropolitan and new Stanford achievement tests, and the Rogers and Bernreuter personality tests. The mean intelligence of the whole group was 103 and the standard deviation 16·8; they were, in fact, neither significantly brighter or duller than non-diabetic children. A psychiatric investigation, however, brought out the striking fact that 32 of 45 children interviewed were maladjusted, and that while diabetes contributed to this maladjustment it was not the only exciting factor. The children admitted to feeling different from their fellows; some responded by aggressiveness, and others by retiring and seclusive behaviour. Out of 9 who felt ashamed of having diabetes 2 thought other children avoided them for fear of catching it. Only 1 boy felt his illness was a punishment, 2 girls were afraid they would be unable to marry, 1 thought it lowered her social prestige and 2 boys were frankly rebellious. Young children were less disturbed and more ready to accept their condition as a part of growing up; of 28 children who had accepted the situation 23 had developed diabetes before the age of seven. Maladjustment was common among those who were undersize for their age, 24 of them being more concerned about their stature than their illness. Intellectual backwardness made 5 children feel inferior, and social factors influenced others; the most intelligent child in the group felt inferior because she had some negro blood.

The parents in some cases seem to have been more affected by the diabetes than the child. One girl said that her mother loved her less since she had developed diabetes; and actually the mother resented the illness and was compensating for her feelings of guilt by extra fussiness over the girl's welfare. This tendency to excessive solicitude was common to several mothers, while others tried to make their children feel they were no different from others and sometimes overdid it. Several claimed that their children had changed as a result of diabetes, and others that the children were more irritable. Irritability could often be traced to hypoglycæmia, but in some cases it was a reasonable response to difficulties in the home. One mother blamed herself for the child's illness and regarded it as the cross she had to bear, which can hardly have made for happy relations with the child.

1. McGavin, A. P., Schultz, E., Peden, G. W. and Bowen, B. D. *New Engl. J. Med.* July 25, 1940, p. 119.

Special Articles

PARATYPHOID OUTBREAK IN GLASGOW

BY E. BLOCH, M.B. Glasg., D.P.H.; AND
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THE distinction between typhoid and paratyphoid was first introduced into Glasgow annual reports in 1925, and till the end of 1939 the average yearly incidence was: typhoid, 39; paratyphoid, 62.

In 1939 incidence was low with 11 typhoid and 48 paratyphoid cases, and during the first two months of 1940 only 3 typhoid and 2 paratyphoid cases were registered. Between the beginning of March and April 12, however, 304 notifications of paratyphoid were received; and 274 were finally registered as paratyphoid infections, of which 270 were treated in hospital. Only 1 typhoid case was registered during this period.

OTHER GLASGOW OUTBREAKS

A majority of the enteric cases registered in Glasgow have been sporadic and any recorded groupings have usually concerned institutions. Only two outbreaks in recent years, both localised, have been attributed to infected food. In the three years 1937–39 the peak months of paratyphoid infections were June, May, and January respectively, each peak being small. In 1936, however, 160 of the year's total of 195 registered paratyphoid cases sickened between Feb. 21 and April 27: at the same time 32 cases from Renfrew and smaller numbers from other neighbouring areas were reported. The 1940 outbreak resembled the 1936 one in being widespread and in not being traceable to a common origin, but it was more explosive in its onset.

COURSE OF THE EPIDEMIC

Onset.—In its rapid rise the outbreak also differed from food-borne outbreaks of enteric infection reported from other localities, but is reminiscent of the water-borne typhoid epidemic of 270 cases at Malton in 1932 (Shaw, 1933). The following table of incidence per week cites the two Glasgow outbreaks, the Malton outbreak, and, as an example of food-borne infection, the Liverpool epidemic reported by Frazer, Glover, and Glass (1937):—

CASES SICKENING IN SUCCESSIVE WEEKS

—	1	2	3	4	5	6	7	8	9	10	Total
Glasgow from 22.2.40 (untraced) ..	7	138	59	23	13	9	3	1	—	—	253 with symptoms
Glasgow from 21.2.36 (untraced) ..	7	19	24	34	34	20	6	4	9	3	160 with symptoms
Liverpool from 18.12.36 (bread)	4	34	45	27	9	5	5	1	1	—	132
Malton from 16.10.32 (water, typhoid)	1	78	64	58	26	11	6	2	1	1	248 notifications

Explosiveness of onset has usually been regarded as a characteristic of water-borne enteric outbreaks. In the water-borne epidemic at Croydon which comprised 310 cases, including 16 secondary cases, the rise was slower than at Malton but was termed explosive by the Ministry of Health (1937). The slow rise of the Hawick (1938) cream-borne typhoid outbreak was included in the arguments against a water origin.

Incubation period.—In 1937, in an institutional outbreak of 6 cases of paratyphoid in Glasgow the period of contact with a carrier before the cases sickened averaged 12·3 days and ranged from 8 to 16 days. In 1938, in an outbreak of 6 cases of paratyphoid in a Glasgow hospital, the intervals between the first contact with a carrier and the dates of sickening were: 9 days (1 case), 10 days (3 cases), 12 days (2 cases). In their report on the Liverpool outbreak Frazer, Glover, and Glass assumed an average incubation period of 12 days. Infection in our outbreak may, therefore, have begun as early as the second week of February or as late as the 19th. The latter assumption would make March 2 and 4 (on each of which dates 33 cases sickened) the twelfth and fourteenth days after infection. It would also imply an incubation period of 3 days for the first case. But Rundle (1929) noted records of such brief incubations and attributed them to massive dosage of infection. Murphy (1937) pointed out that, despite the size of the Croydon epidemic, only one incubation period was ascertainable with comparative certainty. In the present outbreak similar difficulties were encountered. The longest period between the removal of one case from a house and the subsequent sickening of another case in the same house was 8 days. In the 27 familial groups of 2 cases, the period between the sickening of the first case and the sickening of the second case was less than a week in 13 groups, and between 8 and 18 days in 9 groups; while in the remaining 5 groups the interval could not be defined. It was decided to regard an interval of 8 days or more as pointing to the likelihood of a secondary infection in a contact. The difficulty also arose whether to call the symptomless positive contacts primary or secondary. In such an outbreak, cases of primary infection without symptoms could be expected, but these carriers were discovered, through laboratory examination of specimens, some time after the discovery of the original cases in the group concerned.

DISTRIBUTION OF CASES

Geographical distribution.—Removals to hospital which reached a peak on March 19 began on March 4 and totalled 31 during the week beginning on that date. These 31 cases were derived from fifteen of the thirty-eight municipal wards, including four wards on the south side of the Clyde. Ultimately only three municipal wards remained immune—Calton, Kelvinside and Camphill. The first is a densely populated central ward, and the others are residential and more suburban areas. The south side was less affected than the north; with over a third of the city's population it yielded only 52 cases. The most heavily attacked area was a group of 3 wards on the northern riverside—Anderston (in the dock district) had the highest case-rate in Glasgow with 1·269 cases per 1000; Whiteinch (in the shipyard area) came second with 0·729 case per 1000; and Partick West (also a dock district) fourth with 0·613 case per 1000. Together these three wards had a case-rate of 0·856 (68 cases), while for all Glasgow the case-rate was 0·250 per 1000.

Institutional cases.—There were 4 institutional cases which came from three general hospitals. Two cases which came from one children's hospital appeared to be unrelated to one another. The 4 cases had been in the institutions long enough to warrant the assumption that they were infected within the institutions. The institutional population of Glasgow is given as 32,549, so that the institutional attack-rate was negligible.

House-distribution.—Of the 241 primary cases, 237 lived in private houses. The house-distribution of these cases was as follows:—

No. of cases in each house		No. of houses invaded	
1	5	164	1
2	8	23	1
3		2	
4		2	193

There were therefore multiple primary cases in 29 or 15% of the private houses invaded. Including primary and secondary cases, there were multiple cases in 43 of the houses invaded, or 22·3%.

In the Bolton-upon-Dearne water outbreak reported by Shaw (1922), including primary and secondary cases, there were multiple cases in 24·5% of the 94 houses invaded; and at Malton there were multiple cases in 15·4% of the 221 invaded houses. In the Croydon outbreak there were multiple

primary cases in only 1·5% of the 274 private houses invaded. In that outbreak the incidence of typhoid fever among the consumers of the infected water was low (0·775%) as the population at risk was approximately 40,000. In his Malton report Shaw gave attack-rates for water-borne epidemics varying from 0·4% to 8%, including 2% at Bolton-upon-Dearne and over 5% at Malton. If our present outbreak was of water origin, then the attack-rate was even lower, namely, 0·025%, for it would have been necessary to suspect the whole of the city's water supply. Even if, owing to the relatively low attack-rate on the south side, the consumers of Gorbals water (a subsidiary south-side supply) be omitted, the attack-rate among the population supplied by Loch Katrine was still only 0·027%.

Size-distribution of homes.—The size-distribution of the homes of domestic cases appeared to correspond closely with the size-distribution of Glasgow houses as noted in the Housing Act Survey, 1935:—

—	1 apt.	2 apts.	3 apts.	Over 3 apts.	Total
Cases	25	126	78	41	270
Percentage ..	9	47	29	15	100
1935 housing survey percentages ..	13	44	28	15	100

A special scrutiny was made of the larger houses invaded—i.e., over three apartments in size. Of the 41 infections concerned, no fewer than 24 were comprised in 5 familial groups, so that the 41 infections occurred in only 22 houses. The majority of these 22 houses were houses of relatively low rental.

A spot-map confirmed that the epidemic selected the industrial and less well-to-do sections of the population.

Large familial group.—In a family occupying a five-apartment house 9 out of 10 persons were infected, the mother remaining healthy and returning negative specimens. The other 9 persons consisted of 8 multiple primary cases (one of whom sickened on Feb. 29 and the remainder on March 2) and a boy of 8 years who was a contact carrier.

Age- and sex-distribution.—The following table shows that male cases exceeded the female, whereas in recent years male cases registered in Glasgow have usually been considerably exceeded by females; during 1936–39 males formed only 34% of the total paratyphoid cases. Of the epidemic cases 72% were under 20. For 1936–39 the percentage under 20 was only 45% of the total cases.

—	Primary cases										
	−1	−5	−10	−15	−20	−25	−35	−45	−55	+55	Total
Males	1	16	20	23	34	7	14	4	6	—	125
Females	2	16	14	18	30	15	12	6	2	1	116
—	3	32	34	41	64	22	26	10	8	1	241

In discussing water-borne and milk-borne typhoid, Hill and Mitra (1936) wrote—"... variability in the proportional age- and sex-incidence is very great from one epidemic to another whichever the medium of infection. We find water-borne epidemics with a high proportion of adult females amongst the attacked, and similar epidemics with a high proportion of children. Conversely we find milk-borne epidemics with a low proportion of children amongst the attacked or a high proportion of adult males." These differences will depend on the age- and sex-distribution of the population at risk, as well as on the medium of infection. Nevertheless, it is of interest to note that while in the Hawick cream-borne epidemic 76 out of 107 cases (71%) were females, in the Croydon water-borne epidemic only 46·9% of the primary cases were females, and in the Liverpool bread-borne epidemic males exceeded the females.

CLINICAL FEATURES

Secondary cases and contact carriers.—Of the 253 clinical cases in this epidemic 12 (4 males and 8 females) were secondary infections. There were also 21 symptomless contacts (6 males, 15 females). As among the secondary cases, there was thus also a high proportion of females among the symptomless positive contacts. During 1936 there had been 27 contact carriers (10 of whom were registered) associated with 185 cases. If we include these symptomless contacts as secondary cases, we have the following percentages of total infections formed by secondary infections in various outbreaks—Glasgow, 1940 (untraced paratyphoid) 12%; Glasgow, 1927 (milk, paratyphoid) 14·1%; Glasgow, 1931 (ice-cream, typhoid) 8·7%; Malton, 1932 (water, typhoid) 12·96%; and Croydon 1937 (water, typhoid) 52%. These percentages, as one would expect, vary considerably irrespective of the medium of infection of the primary cases.

Clinical features and fatality.—As already reported by Peters (1940) and Anderson (1940) most of the cases showed a sudden onset with vomiting and diarrhœa, and stools either peasoup or green. Many showed rashes which were in some instances profuse. Half of the cases were pyrexial for less than fourteen days, and 17% had fever lasting more than three weeks. The characteristic complications of the disease were few—5 hæmorrhages, 2 perforations, and 1 pulmonary embolism. There were only 3 deaths, although over many years the death-rate in Glasgow for enteric infections has averaged 15% for typhoid and 5% for paratyphoid.

POSSIBLE CAUSES

Cases in other areas and associated diseases.—Towards the end of March, by which time there had been 250 cases in Glasgow, there had been about 140 outside Glasgow, mainly in the burghs of Paisley, Clydebank, Coatbridge, and in the counties of Lanark and Renfrew. In the 1936 spring epidemic there had also been increased prevalence in other parts of the west of Scotland, and the possibility of a seasonal factor increasing the infectivity of the organism was therefore considered.

The following figures for the sixteen principal towns in Scotland show that there was an associated increase of dysentery cases but no associated increase of diarrhœal deaths:—

—	Week ending—							
	2/3	9/3	16/3	23/3	30/3	6/4	13/4	20/4
Enteric fever ..	2	8	142	189	89	36	28	30
Dysentery ..	26	45	87	63	46	34	45	10
Diarrhœal deaths under 2 years	7	11	11	11	7	7	5	6

On the other hand, this increase in dysentery does not apply to Glasgow because the following are the vital statistics for Glasgow for the ten weeks beginning Feb. 18:—

Enteric registrations ..	—	—	6	82	113	53	4	19	7	7
Dysentery registrations ..	6	4	1	4	2	5	4	7	1	6
Diarrhœal deaths under 2 yrs.	4	4	5	9	6	4	6	3	3	6

It is, in fact, well known that enteric usually has its peak in the third quarter of the year although paratyphoid is less regular in this respect; autumnal peaks are also found in dysentery and non-specific diarrhœa, and it is quite against our previous knowledge of seasonal factors to expect a spontaneous rise in a diarrhœal disease during the spring months.

Food.—In conducting the food inquiries, the standard of proof sought was 60%. In the Liverpool outbreak 62% of the patients had consumed bread from the source under suspicion. At Hawick, out of 85 patients who were questioned, 83 had eaten cream often, including 78 who got their cream from one firm. The 2 patients who denied eating cream had worked in this firm's bakery.

Under the supervision of the divisional medical officers, a questionnaire was filled in for each Glasgow case giving the retail supply of several articles of food. The port sanitary staff, the food inspector, and the local food-control office coöperated with the epidemic staff in tracing the supplies to wholesaler, manufacturer, and importer. Inquiries were made regarding illnesses among the employees of many food-wholesalers and food-manufacturers: and visits were paid to several factories to inspect methods of manufacture. Patients were interviewed by medical officers of the public-health department to obtain information concerning food eaten away from home. Efforts were made to ascertain the connexions with Glasgow of cases sickening in other areas. The

alteration of the distribution of common food-stuffs owing to war-time control was examined.

In no instance did the distribution of cases seem to be related to any known distribution of milk or other food, and the medium of infection could not be traced.

Water.—Although the undue preponderance of boys among the cases was noted at the outset and suggested inquiries regarding food-stuffs distributed to cheap cafes, yet the explosive onset of the epidemic also demanded an immediate scrutiny of the main water-supply of the city which comes from two sources, both unchlorinated. The sickening dates of cases pointed to infection in the third week of February: this was the date of the definite thaw following the severe winter (although a lesser thaw began in the third week of January). Although the condition of the water-supply might well have undergone considerable change by the time of examination, specimens were examined from the points of delivery into some households in which familial groups of cases had appeared. The results were all negative. All the chief water-mains in the city contributed to the water-supply of cases.

At the service reservoirs at Milngavie, fæces and urine were examined from all the workers and watchers, and examination for enterica was made of the water from the two reservoirs and also from an adjacent surface water basin. At Loch Katrine examination of excreta from the employees of the water department was carried out, and the effluents from the two sewage plants on the shores of Loch Katrine were also examined for enterica. Throughout all the water-works the health of the employees had been remarkably good considering the prevalence in the city of influenza during January. Neither the water nor the specimens from workers provided any basis for attributing the epidemic to water-borne infection. There had been a general water-shortage in the city due to burst pipes and consequent fall of water-pressure, and at one time the supply had to be increased from 75 million gallons to 85 million gallons per day. The areas which had been conspicuously short of water were not particularly affected with paratyphoid. Nor was it considered likely that the use of water-carts or of stand-pipes in the streets during the frost had been the direct means of spreading infection. Investigations of the water-supplies in the other areas affected were also negative.

Sanitation.—Inquiries at the homes of cases often elicited a history of defective water-supply during January or February, and in a minority there had been an associated defect in the soil-pipe system. In many of the cases, however, there had been no trouble with the water-supply or soil-pipe system throughout the winter. Moreover, the prevalence of insanitary home conditions due to water-supply difficulties antedated the epidemic by some days. Complaints began to reach the water department at the end of the first week of January and reached their peak at the end of the first week of February. Nevertheless, interference with domestic sanitation must have been widespread throughout the city, and the effect of this disturbance must have been aggravated by the blackout war conditions.

It was difficult to isolate either from the business records of city plumbers or from the records of the water department figures that would be an index to the amount of interference with domestic sanitation that had occurred year by year in the winter months. However, a scrutiny was made of abstracts of meteorological records from the year 1925. It was found that, till 1940, the early weeks of 1929 were the coldest of this century. The enteric infections in Glasgow in that year totalled only 81. However, the scrutiny also suggested that the first months of 1936 had been exceptionally cold and that snow and wintry conditions had been prolonged into the spring. It was in 1936 that the other considerable untraced paratyphoid epidemic had occurred. The mean temperature for January and February in 1929 was 33·3° F., in 1936 was 35·2° F., and in 1940 was 32·5° F. The other years from 1925 ranged from 36·0° F. to 41·5° F.

DISCUSSION

In 1940 and 1936 large paratyphoid outbreaks have occurred with the characteristics of spread from a common source but untraced to any common origin. They were accompanied by untraced outbreaks in adjacent areas which appeared to be unrelated to the outbreaks within the city. The Glasgow outbreak in 1940 was of remarkably explosive onset and it is a matter of some concern that efforts to reveal its origin have failed. Whatever this origin may have been, some factor was obviously at work that was strong enough to operate despite the wintry season, for the normal seasonal incidence of diarrhœal diseases is autumnal. If it be assumed that as in droplet-borne diseases there exist many temporary as well as chronic carriers, it might be submitted that this epidemic originated in multiple, widely scattered foci suddenly assuming high infectivity. Yet several cases who remained at home undetected for periods up to two to three weeks yielded no secondary cases so that case-to-case infectivity was apparently low. The results of laboratory investigation of excreta examined for other purposes also suggest that the paratyphoid carrier-rate in the general population showed no increase.

The outstanding collateral environmental circumstance was the great frost with its consequent interference with domestic water-supply and drainage, though infection was not confined to houses whose water-supplies and drainage suffered interference. Most of the cases arose in small houses in the more densely populated industrial areas, where apart from increased opportunities of spread of infection from person to person, probably there was also an enforced degradation in standards of personal hygiene. The outbreak shows the threat that may reside (even in a locality where enteric infections have long remained within "residual" limits) in a temporary deterioration of the sanitary environment. The blackout must have aggravated the general sanitary disturbance. There is some evidence that the weather at the beginning of 1936 was of exceptional severity and there was, no doubt, disturbance in the sanitary environment then, though less than in the first months of 1940.

SUMMARY

Glasgow has experienced its second untraced and considerable spring outbreak of paratyphoid within five years. There were 274 infections, of which 12 were probably secondary and 21 others were asymptomatic.

Features of the outbreak were:—

Its explosive onset with 138 cases sickening in the second of its seven weeks' duration.

The excess of males over female primary cases.

The unusually high proportion of cases aged under 20 years (72%).

The high proportion of invaded houses with multiple infections (15% for primary cases, 22·3% for all infections).

The almost complete limitation of the epidemic to the less well-to-do sections of the population throughout the city.

The concurrence of apparently unrelated outbreaks in surrounding areas.

The failure of investigations to reveal its origin.

The weather in the early months of 1936 and of 1940 was exceptionally severe. The effect of the weather on sanitary conditions in 1940 was aggravated by the war-time blackout.

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WITH a view to avoiding the importation of glycerin British producers have instituted a system of rationing for supplies to manufacturers and wholesale distributors. They are discouraging the use of glycerin in the manufacture of tooth-pastes and toilet articles generally and are reducing the amount released for medicinal purposes. An official medical committee is now investigating the question of substitutes, and in the meantime doctors should avoid the prescription of glycerin where possible. The rationing does not imply that there is any danger of a dearth of glycerin; it is simply intended to limit home consumption to home production.

WAR AIMS

A NUMBER of men and women, more or less prominent in the political world, have lately set out their views as to the kind of world order they would establish after the war, if they had their way. Their book[1] illustrates the difficulties of speedy action by democratic methods; for, while all the writers are agreed that we should be prepared with clear and definite ideas as to the uses we shall make of our ultimate victory—our peace terms and our post-war aims—they are far from being in agreement as to how this shattered world may best be remoulded nearer to the heart's desire. Some readers will be inclined to echo the celebrated opening phrase of the cookery recipe attributed to Mrs. Glasse: "First catch your hare." Others, more complacent, will say that our only job at present is to smash Germany, and then to let things settle themselves. It is certainly unfortunate that so many of us are actuated by ideals and motives that are mainly negative, protective, preservative; whereas those of our opponents are positive, acquisitive.

The contributors to this symposium are comparatively young; that is to say, they were born in the present century. All the political parties, except the Communist, are represented. The editor himself is a Conservative, as is also Major Victor Cazalet; Sir Richard Acland is a typical modern Liberal; while the Earl of Listowel, Mr. John Parker and Mr. Richard Stokes are prominent members of the Labour Party. The two women contributors are the Baroness Ravensdale, eldest daughter of the late Lord Curzon, and Miss Irene Ward, Conservative member for Wallsend-on-Tyne. Two of the freshest and most stimulating essays are those of Mr. Stokes, who is a Socialist and a Roman Catholic, and Mr. David Astor, who is still in his twenties. But here is a quotation from the contribution of Captain Alan Graham, incidentally the oldest of all the writers, being in his forties and therefore getting nearer to the de-bunking age. "We were told in 1914, as we are told today," he says, "that it was for 'democracy' that we were fighting and against autocracy, and yet we had for our faithful ally the Russian Tsardom, while the German Social-Democrats, having voted in 1913 for that year's colossal increase of the army of the German Empire, continued to support it as long as ever it looked like winning! In those four years of war the average British soldier was certainly not consciously dying for 'democracy,' whatever epitaphs demagogues may have placed upon his memorials. The average British soldier of 1914–18, if able to give any articulate reason as to why he was then fighting, would have said 'to stop Kaiser Bill from bossing the world!' In other words he was, although most probably unaware of it, fighting for British against German Imperialism. He certainly, unless singularly ignorant of human nature as well as of all recorded history, could not have imagined that he was fighting a 'war to end war,' the other popular and equally unreal slogan of those days."

In certain well-to-do and influential circles there is a hope that after the war we shall be able to return to the way in which we lived in 1913, or at any rate in 1939. Fortunately that is impossible. The leading article in the *Times* of July 18 recognises this.

> "In the European order of the past 20 years Hitler finds one of his easiest targets. . . . He finds another in the contradictions of our social and economic system. German propaganda in recent weeks has been treading familiar ground. The chronic unemployment, the inequalities of social privilege and vested interests, the burning of wheat and coffee while men went hungry, the senseless accumulation of gold in Fort Knox, Kentucky. . . . Much harm may be done to our cause, both in Europe and overseas, by the insinuation that we stand for the old order and that our only aim is to restore the status quo in Europe and to maintain it at home."

> Ægrotat Dæmon, monachus tunc esse volebat.
> Dæmon convaluit; Dæmon ut ante fuit.

True patriotism is not to be confused with that egoistic nationalism which is at the root of the present war, as of most other wars. Rather is it a kind of pride and affection which make a man not only delight in his country's glory but also wince at her shame. Our concern is primarily with that country whose course alone we are called on to direct. As Pythagoras said, "The best thing we can do for a child is to make him the citizen of a country with good institutions." England has a character, a tradition, a personality as distinct as are the qualities of individual men and women. Real patriotism will endeavour to give full expression to this personality, while respecting as of equal value and having equal claims the personalities of all other nations. But a policy for England should be a genuine English policy—not a French or a Russian or a German one.

There must be no narrow bigotry and inhospitable exclusiveness in our definition of who are the English. They are the people, whatever their racial source, who have made England their home. Let us exclude whom we will; but once having admitted a man or a woman to citizenship, we must show our dignity and national good breeding by henceforth regarding him or her as one of ourselves. Our laws, it is true, still make no distinction; but some of us manifest a smaller spirit. Let the true-born Englishman consider the blood of which he is made—Celt and Dane, Teuton and Norman, Dutch and Huguenot. England is able to assimilate them all. It seems, indeed, that England can make English people of all who come.

1. After the War. A Symposium of Peace Aims. Edited by William Teeling. London: Sidgwick and Jackson. Pp. 198. 12s. 6d.

ECONOMY IN ESSENTIAL DRUGS

MORE HINTS TO PRESCRIBERS

ANOTHER series of recommendations of the advisory committee (see *Lancet*, Sept. 14, p. 340) deals with drugs which they consider essential for certain purposes but whose use should be restricted. In their opinion boric acid in boric lint is wasted. Stocks of agar should be reserved for bacteriological media, and for other purposes ispaghula should be prescribed instead. A substantial volume of alcohol would be saved if tinctures were replaced by concentrated preparations. The limited supplies of orange peel which are available for galenical preparations should be used with strict economy. Where possible aluminium hydroxide, magnesium trisilicate, kaolin or chalk should be prescribed in place of bismuth salts. Borax should be used sparingly. Caffeine should be omitted from compound tablets such as compound aspirin tablets, and elsewhere nikethamide, leptazol and amphetamine can partially take the place of caffeine and sodium benzoate.

The committee suggest that capsicum should only be used in the manufacture of capsicum wool and that for other purposes mustard should be substituted. Cloves should be reserved for the distillation of clove oil. Dioxyanthranol is recommended in place of chrysarobin, proflavine or acriflavine in place of iodoform, and proflavine, acriflavine, trinitrophenol, crystal violet or brilliant green in place of iodine. They say that preparations of ipecacuanha as expectorants and emetics are not essential and advise that in allocating supplies of ipecacuanha preference should be given to the manufacture of emetine. Jaborandi should be reserved for the manufacture of pilocarpine and for most purposes physostigmine should take its place. As substitutes for santonin the committee propose hexylresorcinol. Concentrated solution of ethyl nitrite is recommended for spirit of nitrous ether. The use of all syrups should be discouraged and compound syrup of iron phosphate should be reserved for children. Sodium salts should be substituted where possible for potassium salts, the compounds specially mentioned being the bicarbonate, bromide, chlorate, citrate, hydroxide, iodide and permanganate. Economy is called for in the salts of mercury—the subchloride, oxycyanide, perchloride, yellow oxide and red oxide—because the metal has to be imported, and phenolic antiseptics of the chlorinated phenol type are suggested as substitutes for corrosive sublimate. Sodium salts should be prescribed where possible for magnesium carbonate, oxide and sulphate.

The importation of cinchona, the committee say, should be restricted to the supplies required for the manufacture of quinine and its use as a bitter should be avoided. Production of cinchona within the Empire should be encouraged, as should that of cascara sagrada and liquorice.

which should be used sparingly in the meantime, Substitutes for glycerin are under investigation. Indian podophyllum (*P. emodi*) is recommended instead of the American drug (*P. peltatum*), and quillaia should be employed with care. In the committees' opinion oil of chenopodium is not essential in Great Britain and they suggest thymol or carbon tetrachloride as substitutes. Economy is called for in certain substances, which are under government control—malt extract, cod-liver oil, olive oil, honey, soft paraffin, liquid paraffin (whose "use should be discouraged"), lanolin, benzoated lard, starch, dextrose, acetone, citric acid, tartaric acid, cream of tartar and sodium citrate. Vitaminised oil is recommended in place of cod-liver oil and arachis and other vegetable oils in place of olive oil. Where liver extracts are required the committee say that injection is the most economical and effective method of administration.

In England Now

A Running Commentary by Peripatetic Correspondents

WHEN I joined the E.M.S. a year ago I asked for a tin hat, since I saw that the clerks in the hospital to which I was then attached all had them; they were not, like the doctors, expected to go out in emergencies. I was told that they would be provided in time when more became available. I have asked again, at odd times, but always received the same answer. I must admit, however, that I did not ask sufficiently to make myself unpopular. With the onset of this blitzkrieg I thought it wise to ask once more as firmly as possible. Before I did so I enquired of the other doctors practising in the same house if they possessed them; none of them did. A fair cross-section of those in my immediate vicinity, therefore, had not been able to obtain hats. In answer to my demands, my sector officer wrote and told me that no tin hats were available and advised me to buy one from one of the big stores. Not only have they sold out at the present moment but there is no guarantee that the tin hats they sell are as good as the service ones. I saw the advertisement advising medical men to obtain tin hats from their local war committee so I went to 31, Harley St. and asked the receptionist to put my name down on the list. I was told that I should have to wait, because 1000 Home Guards had to be provided with them first. In the meanwhile, a house opposite the flats where I live was bombed one night and collapsed with a man under it. I stood by for some five hours, without any protection whatsoever, waiting to give this man attention. I have asked other people if they have tin hats, but only one doctor has told me that he has had one issued from his sector. Yet I see that every W.A.A.F., every A.T.S., every shelter marshal has a tin hat and even civilian members of the B.B.C. have tin hats. These people have no necessity to go out in raids. A doctor is worth less than a cook in the A.T.S. apparently. I have paid my seven-shillings-and-sixpence to the local war committee and the local secretary has written to me telling me that the list is really closed but a supplementary list is being prepared. In the meantime my head is to be exposed to any odd piece of shrapnel dropping from the skies.

* * *

A great drawback to one-earedness is that one loses all sense of the direction of sound. I find this particularly galling now when one so often wants to see the aeroplane one hears. I can only approximate to the direction by rotating slowly and finding where is the loudest noise, a clumsy and undignified method. Probably I have had one stone-deaf ear since early childhood, although almost incredibly it was not spotted by me or anyone else till I was eighteen. I have compensatory acuteness of the other ear, so that no-one notices it, although they often notice my manœuvres to get into a good strategic position. One result of the compensation is that I am very sensitive to noise; I cannot concentrate if people are talking, for the good ear has been trained to demand all my attention. It has an increased awareness, and when its owner is walking along a country lane it is able to distinguish the rustlings in the wind of the different species of trees. At night if one turns on one's good ear the world of sound is nearly blotted out, and that's a great advantage. One also gets a faculty for reconstructing a sentence from a word or two and the intonation. Sometimes one makes a howler. At dinner on board ship I was left alone with a lady who waxed confidential. "You know, my husband was a great . . . ." I guessed "gardener" or "golfer," and said "How jolly." She drew herself up, "It wasn't jolly at all—he was drunk on my wedding night, and I've never smiled since."

A mechanism I have never understood is that by which, if you are watching a person's mouth, you can better hear what they are saying—or singing. If you watch one of the choir in church, for instance, you seem to hear him almost to the exclusion of the others. It can't be lip-reading for Edward Grey had the same experience when watching a spotted flycatcher through binoculars, and I have often confirmed this with other birds.

* * *

On Monday Nannie remarked at breakfast that the purchase tax started tomorrow and if we wanted any shoes or stockings or a new hat we had better get them today. There was some discussion on the ethics of this course. Was it quite nice to do the Chancellor down when it seemed so easy, particularly since the shops had patriotically avoided mentioning the tax in their advertisements? In the end we bicycled into the town, and in company with many others bought a pair of shoes each and a supply of socks. But none of us felt very proud of it, and it was a relief on Tuesday to read in the *Times* that the tax would be brought into operation as soon as possible but the date had not been fixed.

* * *

A small boy took a puss-moth caterpillar to church in a match-box; it escaped; he was reproved; feeling that kindness to animals would appeal to grown-ups, his excuse was that he thought it would enjoy the outing. It is difficult to share mental pictures with others, one can only do it with words, which are coarse brushes and paint differently with other people; but by bribery, patience, and by casting off for a little while the crust of years I did get a glimpse of what was going on in that boy's mind during that Sunday service.

Two preliminary episodes must be recounted. The first is that some days before he had watched men shooting driven partridges; they were dressed in plus fours, one of them at any rate was smoking a cigar, and they were such deadly, nonchalant shots that they made a vast impression on him. The second is that in the school chapel in the previous term a preacher had said that if you look for the nasty things of life you will always find them and find little else, and had illustrated this by pointing out that if you listen for the sibilants of the esses in song or speech, you will hear them and them alone. The boy, discarding the moral, had pounced on this interesting discovery. Well, there we are. All an outsider would have seen was a small boy in church, his hot hand clasping a match-box in which the movements of his pet caterpillar, Buddy, could faintly be discerned. Really, what was happening was that he and Buddy, both in plus-fours and smoking cigars, were shooting sibilant partridges which were coming over in enormous numbers—"the scripture moveth us in sundry places," for instance, is two brace—and were shouting to each other "O, good shot, Buddy," "O, splendid right and left, Archie!" I gathered neither of them ever missed.

* * *

The Greeks had no word for it but the Romans called it Coccium. Did they laugh inanely at one another when Coccium cropped up in the conversation, as many people do now when the town is given its modern name—Wigan? I rather think they did. There seems to be something intrinsically funny about both names, and so the ancient town has suffered by a doubly unkind dispensation of Providence. Music-hall artists throughout the English-speaking world recognise in the mere mention of Wigan an unfailing source of merriment, and no matter whether his audience be in the metropolis or the Antipodes or where you will, the comedian can depend upon this gag eliciting convulsive laughter. Wigan can claim a link—a slender one perhaps—with the Royal College of Physicians of London. The founder of the college was Sir Thomas Linacre, and he

seems to have had some connexion with the town, for Wigan grammar school library is known as the Linacre Library and one of the school houses is called after him. What his association actually was with Wigan remains obscure, and I imagine that we should look in vain for enlightenment in the early minutes of the college, although the erudite director of the Wigan public libraries might have been able to provide Professor Topley with some useful information for his Linacre lecture. But it is of no avail for Wigan to call up the giants from its long and illustrious past to defend it against the mockers. "We are all good and bad in parts," says Dean Inge, and the same applies to towns, including Wigan, but such is this town's comical name that men will continue to laugh at it "till time and times are done."

Parents ambitious for their children should consider not only the names of their offspring but also the names of the places in which they are to be born. What an asset it must be to claim for one's birthplace a town with a beautiful name, and such names abound in England. Think of Sevenoaks, Melton Mowbray, Leamington, Malmesbury, and Shrewsbury. These are the names that tumble about one's ears to the music of Edward German and the prose of Mary Webb. And what is written here of England could easily be applied to other parts of Britain. I remember a woman medical officer at a Birmingham fever hospital confiding in the mess that "she was nearly born in England." The expression of relief at disaster narrowly averted was easily explained, for in spite of her English domicile her inflection left no doubt in the mind that Scotland, aye and Glasgow too, claimed her for their own.

* * *

I was doing a locum in a lovely English village. The children played on the village green and red chestnuts blazed beyond. The telephone goes. The local policeman speaking. Can he bring a girl and her mother up? Assault case. A girl of twelve and a woman come into the surgery, where the child tells of a hedgerow seduction by an ice-cream vendor. She displays neither shame nor horror, but talks impersonally and mechanically as though reciting "The Charge of the Light Brigade." I find one small bruise, vitally placed. The woman draws me aside. "I'm not really her mother—just her foster-mother, but she doesn't know." If I had been more astute I think I might have guessed that; too much detachment between these two.

The gardener here and I have become "soil brothers." I got him some Glastonbury thorn to bud on his hawthorn, so that they will bloom in December. I mention that because he tells me the other side of the story which he got via the boot boy via village boys still at school. This ice-cream barter had been going on for some time. The boys were furious because the girls had feasts without payment of money. They talked and it got to the ears of the policeman, but he couldn't do anything until he got evidence. Finally this girl informed, not because of her injured modesty, but in anger and revenge because the man had tricked her. At the police-court in the county town, where a very dapper inspector was definitely the master of the ceremonies, I saw this monster of the stop me and buy one brigade. He was 43, a poor dilapidated little rat of a man. I gave my evidence. Yes, the bruise might have been caused like that. Could it have been caused bicycling? Yes, but I should say it's unlikely. There were two magistrates and I noticed that one of them was looking at me—well, admiringly. It gave me confidence. Later the P.C. gave his evidence and I noticed that he too was being gazed at with admiration. Then I saw the magistrate raise his arm. Idiot—he had paralysis agitans and the admiring gaze was Parkinson's mask! The inspector made the presiding magistrate say that the prisoner would be remanded so that his mental state might be looked into. "Can I have bail, mister? It was all the girl's fault. I'll be a good boy. Can I have bail, mister?" It was the cry of an urchin of ten and I should think his mental age was less than the girl's.

I had an evening visit from the parson, much upset—terrible thing to have been going on in his village. In a way he felt personally responsible. I sought to assuage. In growing up we go in synopsis through the history of man, and the stage just before puberty is like the stage just before civilisation. I can well imagine the Iceni women selling their charms to the Roman legionaries for ration or ornament. I don't believe he listened to me, he was too distressed. "But many of these children are in my Sunday school and come from really nice homes. To me it's absolutely incredible." Yes, two or three thousand years takes a lot of bridging.

I left that locum soon afterwards, having been bound by oath to come back if the case went to assize. I never heard anything more about it officially, but a few months later I was driving through that country town, and saw that dapper inspector on the pavement. I went up to him, told him who I was, and asked him about the case. "We get so many of these cases I'm not really quite sure," he said doubtfully. "O yes, I remember. They couldn't bring him in as mentally deficient and I think he got four months." There is no point or moral in this story, but I think it still is one of the most picturesque villages in England.

AIR-RAID SHELTERS SCRUTINISED

THE breathless activity of the committee on conditions in air-raid shelters should give the lie to the belief that we are a dilatory nation. The committee was appointed, under the chairmanship of Lord Horder, on Friday, Sept. 13, and completed its survey and presented its report by Wednesday, Sept. 18. The other members of the committee were Dr. M. D. Mackenzie, a medical officer to the Ministry of Health, Mrs. Creswick Atkinson, R.R.C., technical adviser to the Women's Voluntary Services, Sir Wyndham Deedes, chief warden of Bethnal Green, and Sir Alexander Rouse, chief engineer to the Ministry of Home Security; Mr. F. G. Downing, of the Ministry of Home Security, was secretary. The recommendations of the committee are being implemented by an interdepartmental committee of the Ministries of Health and Home Security, under the chairmanship of Mr. William Mabane, parliamentary secretary to the Ministry of Home Security. The recommendations of the Horder committee were chiefly concerned with overcrowding, and the control of shelters from the medical point of view. Sir Edward Evans, London Regional Commissioner for Civil Defence, has been appointed to supervise the improvements in London's shelters which are now being put in hand.

ICINE AND THE LAW

Miner's Nystagmus

PREDISPOSITION to nystagmus was discussed in a recent case in the Lichfield county court. Shotton, the applicant, had been certified as suffering from the disease in 1937. Four months later he registered at the employment exchange and eventually obtained work as a commissionaire. He continued to receive £1 a week compensation till March, 1939, when an examination indicated that he had recovered inasmuch as there was no oscillation of the eye-balls. The respondent employers, the Cannock Chase Colliery, then gave notice to terminate the payments. Medical evidence for the applicant stated that there was an increased susceptibility to nystagmus; Shotton himself said that, if he bent down and rose quickly, an attack of nystagmus would follow. On the other hand the medical witnesses called by the employers distinguished the true case of susceptibility to second attack from the other cases where there was no such susceptibility but where a second attack might be induced by some extraneous cause such as domestic worry or influenza. They placed the applicant in the second class and said that recurrence would not be due to the original attack. The judge referred the case to a medical referee. On the latter's report that Shotton was now free from the disease, and that any fresh attack would be due to defective nerve control, the court declined to make an award.

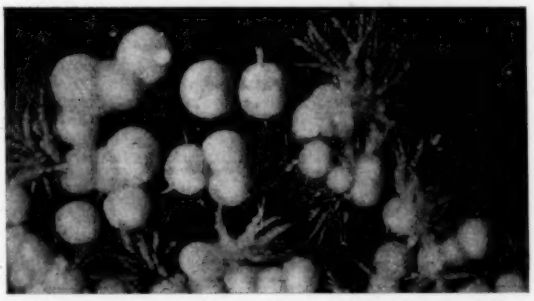
Mr. C. W. MAUDSLAY who has retired from his post of principal assistant secretary to the Board of Education will continue in part-time employment, visiting areas where the proposals of the local education authority for the provision of meals and milk for school-children do not appear to meet fully the needs of the area.

Letters to the Editor

VAGINAL DISCHARGE

SIR,—I was extremely interested in your leading article of Sept. 7, particularly with regard to monilia infection.

At both my venereal-disease clinics at the Royal Free Hospital and the Salvation Army Mothers' Hospital many patients attend for examination of vaginal discharge in pregnancy and for some years a condition has been observed which is undoubtedly a clinical entity. A number of patients complained of discharge accompanied by soreness and irritation—at times intolerable irritation robbing the patient of sleep and rest. On examination, as I have implied, most of these patients were found to be pregnant, but with increasing recognition of the condition not all; the condition does occur in non-pregnant patients, but much more rarely. There is soreness, redness and sometimes swelling of the vulva, the soreness and redness extending in severe cases to the perineum and groins and even progressing to excoriation. There is no sign of infection in the urethra, Skene's ducts or Bartholin's ducts, and on passing a speculum the vagina and vaginal fornices are found coated with a thick pasty or cheesy discharge varying in colour from white through shades of yellow to a pale green; through this discharge appear the bright red rugæ of the vaginal walls, except in the few cases in which the discharge forms a semi-solid mass filling the whole of the vagina. When the discharge is swabbed away the cervix is found not to share in the inflammatory process. The condition is more frequent in hot weather, and fair-skinned women are more often and more severely affected than dark.



Vaginal secretion; 3 days' anaerobic culture. Thomson's medium ×20. Shows two varieties of monilia colonies.

From a particularly severe case at the Salvation Army Mother's Hospital I sent specimens to Dr. Thomson of the Pickett-Thomson Research Laboratory and quote his reports (Oct. 30, 1939).

Direct examination (gram-stained smear) shows epithelial cells and some pus cells and large numbers of secondary organisms—chiefly diphtheroids, staphylococci and some small gram-negative bacilli. Fair numbers of yeast-like cells and mycelium are present.

Dark-ground examination negative for *Trichomonas*.

Culture.—Shows a heavy and profuse growth on blood-agar and hydrocele agar of a yeast-like mycelium.

I am sending you slides of (1) direct examination, and (2) cultural, as they are interesting and striking. The presence of these yeast-like organisms is suggestive of the condition being due to a mycosis. Strange to relate I found the attached cutting in the *Journal of the American Association* which just arrived this week and entirely corroborates this (*J. Amer. med. Ass.* 1939, **113**, 1508).

In December Dr. Thomson kindly sent me the accompanying photograph of the culture from this case showing two varieties of monilia colonies.

I have found these cases respond very well to treatment with vaginal Stovarsol; if the patient can easily attend hospital I order a low-pressure douche of sodium bicarbonate (1 drachm to the pint) with the insertion of 1 stovarsol tablet and a small tampon; if daily attendance is difficult the patient is instructed to bathe the vulva with the solution of bicarbonate of soda and to insert the stovarsol tablet after lying down in bed and after having carefully cleaned her fingers and hands. When there is much vulval irritation I order a lotion of 3% phenol in boric, but in the majority of cases this is not necessary since the response to stovarsol is immediate. It is a pleasure to see these patients a week after treatment has been instituted—the soreness and irritation have gone, and the patient can walk in comfort and sleep in peace.

I must add a word of warning. As a rule the relief is so great and so immediate that there is a tendency on the part of both patient and medical attendant to give up treatment too quickly. In the majority of cases I prescribe vaginal stovarsol nightly for two weeks, then drop to one tablet on alternative nights for three or four weeks, and then one as required for four to six weeks.

A great many of the cases have been examined after delivery when no signs of the infection can be found.

Dr. Matters refers to the staining due to Bonney's blue paint, but I have found the same objection to silver picrate.

I would like to express my appreciation of the interest shown by Dr. Thomson and my thanks to many medical officers in charge of antenatal clinics who have sent me patients.

Harley Street, W.1. MARY MICHAEL-SHAW.

SIR,—I have read with interest the review of Matter's paper on vaginal discharge in your leader of Sept. 7. With regard to so-called monilia vaginitis, you say that "it remains to be seen whether this fungus is a common cause of vaginal discharge in the British Isles." In my experience it is a common cause and is only considered uncommon because its clinical features and method of diagnosis are unknown, even to many gynæcologists.

During a year's work on leucorrhœa, I became particularly interested in "vaginal thrush" and met with many cases. The results of the work have been published in collaboration with Colonel W. Glen Liston (*Edin. med. J.* 1940, **47**, 369; *J. Obstet. Gynæc.* 1940, **47**, 109) and summarised in your columns (*Lancet*, 1940, **1**, 1174).

Among 200 cases of leucorrhœa in pregnancy we found 49 cases of vaginal thrush—i.e., almost 25%. The diagnosis was established by staining by Gram's method a film taken from one of the whitish patches which characterise the condition; we found it important that the film should be made from one of these whitish patches, since in several of our earlier cases the diagnosis was missed at first owing to the film being made from the posterior fornix as a routine.

As regards treatment, we found that bi-weekly painting of the whole vagina, external genitalia, thighs and pubic region with 2% aqueous gentian violet is usually successful, and if it does not always cure it never fails to relieve the distressing pruritus from which these unfortunate women suffer. The wearing of a pad for a day after application obviates any staining of the clothing.

Chesterfield. LEWIS G. CRUICKSHANK.

SIR,—Increasing attention is being given to the monilia group of infections. In the last twelve months I have had 27 cases amongst patients attending the discharge clinic of the Middlesex Hospital. The appearance on clinical examination was diagnostic in most of these cases and monilia was found in swabs taken from the neighbourhood of a typical patch of vaginal thrush. Eight of the patients were pregnant. In one case large numbers of monilia were found in a catheter specimen of urine which contained a few pus cells but no other organisms. The routine Negatol treatment as previously described for trichomonas infection was used in the first 16 cases and the results were satisfactory. The remaining cases have been treated by means of Monsol (1 in 200) douches. This latter method was suggested to me by a colleague who obtains excellent results with this substance in the treatment of oral thrush. In the treatment of acute gonorrhœa I have recently been insufflating the upper vagina with powdered sulphanilamide using 3 g. on each of two occasions within the first ten days, this in addition to the routine administration of M. & B. 693 by mouth. I was prompted to try this by

the reported efficacy of packing wounds with powdered Prontosil, but I have not done it often enough to justify any conclusion.

Middlesex Hospital, W.1. O. LLOYD.

TREATMENT OF WAR NEUROSES

SIR,—Dr. Pegge states that as psychiatrist to a group of four hospitals in the London area he has been asked to see a number of psychiatric casualties (by which he apparently means neuroses) at only one of them, and he wonders why such cases should be absent from the other three. I suggest that they were present in equal numbers, but that they were at once cured by the medical officers who saw them on admission. Dr. Pegge does not seem to realise that others besides psychiatrists can practice the simple forms of psychotherapy required for these acute cases.

Oxford. ARTHUR F. HURST.

NEUROTICS IN THE FORCES

SIR,—Lightheartedly, in his letter to THE LANCET of Sept. 21, Dr. Hendry sets out to tell us what is reasonable and what is not reasonable doctrine concerning the neuroses. He declares that it was the general experience of regimental medical officers in the last war that soldiers who had broken down in the firing line should not be returned to it, and if they were they had to be "very carefully watched, guarded and supported in order to keep going." As a former regimental medical officer and later as "shell-shock" specialist to one of the armies in France in the last war, responsible in both positions for sending shell-shock cases back to the firing line, I have on more than one occasion challenged the accuracy of this statement and asked for the evidence on which it was based. Will Dr. Hendry, as he speaks with such confidence, produce it and settle the point once and for all? The idea of a regimental medical officer carefully watching, guarding and supporting returned cases of "shell-shock" in his unit is not a little entertaining.

London, W.1. FREDERICK DILLON.

SIR,—Your leading article of Sept. 7 urges that prophylaxis of neurosis is likely to reward investigation. Successful physical education is one item in this prophylaxis and must help to create a state of health which will react quickly back to normal should it be assailed by accident or disease. But physical education cannot achieve its aim of contributing to better health if it is divorced from general education. In boys between eight and fourteen much can be achieved by treating nervous instability with skilled physical education either individually or in small groups.

This instability which may be the precurser of adult neurosis manifests itself in many ways—e.g., general muscular imbalance shown in poor postures and bad movements, choreiform movements, general untidiness, tachycardia, asthma. Alternatively, careless habits of posture and movement may predispose to nervous instability. In treating these conditions in boys, one aim is to improve function by training, another to improve coördination by insisting on accuracy in posture and in the detail of all movements. An efficient and accurate physical mechanism capable of reasonable accuracy in sensation and in action should help to create mental confidence. It seems to me to be failure if boys, or for that matter members of H.M. Forces, leave their physical-education classes to relax at once into bad postures and walk away with feet in the valgus position.

Sutton, Surrey. A. L. KERR.

DIPHTHERIA DIAGNOSIS BY POST

SIR,—I feel that the case cited in your annotation (Sept. 21, p. 367) is hardly a fair one. A doctor who posts a swab on a Saturday evening cannot, however efficient the service, expect a reply in reasonable time, and the responsibility for the death therefore rests with him. Every efficient private laboratory has a service to pick up urgent swabs, either from the doctor himself or from the railway station to which it can be sent at once by passenger train, and these swabs are planted immediately. It is often possible to examine direct films at once.

The diagnosis of diphtheria by means of swabs is a highly skilled operation, and an experienced and efficient operator at a small distance is better than a second-rate one on the spot. As far as the use of tellurite media is concerned, the delay resulting from this occurs in any case, and the use of a more rapid diagnostic method in parallel should never be omitted. The emergency public-health laboratories of the Medical Research Council have not solved the problem of speed, for instances are already apparent of work being sent to much greater distances than previously. Public-health authorities have even been canvassed by these laboratories to send their pathological work to a town at a distance when this work was already efficiently carried out in the town itself, which seems to be in violation of the plea made at their inception by the Ministry of Health, that they were intended to supplement existing facilities and not to supplant them.

London. J. W. SHACKLE.

DEATH IN INFANTILE ECZEMA

SIR,—In a recent annotation (*Lancet*, June 29) the occasional sudden death of infants with eczema is left unexplained. I suggest that death in these cases is caused by complete exhaustion of the adrenal glands as a result of an acute infection, following a brief initial stimulation which produces a transitory pyrexia. This could probably be proved by bacteriological examination along modern lines before death, and a complete post-mortem examination immediately after it. In allergic subjects there is underaction of the adrenal-sympathetic system with relative vagotonia. An acute infection causes the allergic symptoms temporarily to disappear, partly, no doubt, owing to stimulation of the adrenals; but subsequent exhaustion of the adrenal-sympathetic system exacerbates the symptoms with a fall of blood-pressure and sometimes increased pigmentation of the skin. Extreme cold has the same effect. One of my patients who suffers from prurigo and asthma relapses whenever the weather is cold; her systolic blood-pressure falls to 80 mm. Hg, and her skin becomes deeply pigmented. Improvement, in her case, always follows injections of adrenal cortical hormone. Cramer[1] showed that if a normal mouse is exposed to moderate cold the adrenal and thyroid glands are stimulated and vigour is increased, but that if it is exposed to extreme cold the glands become exhausted and temperature and blood-pressure fall; if the exposure is prolonged the animal dies. Patients with relative insufficiency of the thyroid-adrenal sympathetic system (many of whom are allergic) are depressed and made relatively inactive by even moderate cold.

Apart from instability of this system, eczematous infants tend to have periods of fluid retention in the tissues; symptoms at these times are active and subside temporarily with diuresis. Allergic patients often show alternation of symptoms: when their asthma is troublesome, for example, their eczema is quiescent and vice versa. They also tend to become sensitised to various exogenous and endogenous allergens. Keeping these facts in mind, I submit my comment on the main features of these fatal cases as described by Twiston Davies[2]:

1. "The accident occurs during the first year of life"—that is, before some stability of the thyroid-adrenal-sympathetic system and immunity to common infections have been established.

2. "Undernourished infants are not so susceptible as large fat infants with or without a tendency to ricketa."—Actually it is a question of fluid retention, not over-nourishment. The skin, subcutaneous tissue, and mucous membranes are watery and in some cases the œdema even causes pitting or pressure. The wateriness of the mucous membranes predisposes to infection with catarrhal organisms.

3. "Most of the cases occur in the spring"—that is, when all common infections are most prevalent.

4. "Nearly all, if not all, cases occur in hospital or away from the mother."—A considerable proportion of patients of all ages develop febrile infections from five to ten days after admission to hospital. However unsatisfactory home surroundings may be, active infections among members of the

1. Cramer, W. Fever, Heat Regulation, Climate and the Thyroid-Adrenal Apparatus, London, 1928.
2. Twiston Davies, J. H. *Brit. J. Derm.* 1940, **52**, 182.

household will occur only at relatively long intervals, and the odds in favour of a baby being exposed to such an infection are much greater in hospital than at home.

5. "The accident usually occurs within the first few days of hospitalisation."—Dr. Davies found that 70% of deaths occurred within 10 days and 50% within 4 days of admission—that is, within the incubation period of common infections.

6. "The onset of the complication is sometimes heralded by improvement of the eczema."—This may be due partly to adrenal-thyroid stimulation at the outset, and partly to the alternation of symptoms characteristic of allergy.

In a typical case the initial pyrexia, which may reach 103° F. or more, can only be due either to an infection or to hæmorrhage into the adrenals; such hæmorrhage may occur either in association with acute bacterial infections or in their absence. Allergic children are apt to develop alarmingly high temperatures as a result of infections which would evoke but a slight temperature in normal children. Recovery may be rapid and complete, and Dr. Davies remarks that "the child may even become comatose and yet the following day present its normal aspect and take its food as usual." This abnormal reaction to common infections is, I think, an example of adrenal-sympathetic instability; and it is logical to suppose such an intense response might lead to rapid exhaustion of the adrenals.

Dr. Davies suggests that adrenaline, given promptly, can be of value in treatment; probably the effect would be enhanced by combining it with cortical hormone. Post-mortem examination may reveal no obvious cause of death, but the effects of so recent an infection would hardly be manifest to the naked eye, and changes in the adrenals could not be demonstrated unless they were removed immediately after death and examined by Cramer's method.

London, W.1. H. W. BARBER.

PSYCHIATRIC COMPLICATIONS OF HYPOGLYCÆMIA

SIR,—Surgeon Lieut.-Commander Anderson's paper in THE LANCET of Sept. 14 raises an important question. Does hypoglycæmia produce permanent cerebral lesions in those who survive? If so insulin is indeed a dangerous drug, for most diabetics, both children and adults, have severe hypoglycæmic attacks from time to time. I know of only one case, reported by Campbell,[1] in which there was profound mental derangement after hypoglycæmia. A woman of 47 made a dramatic recovery from status epilepticus (blood-sugar 30 mg. per 100 c.cm.) immediately after the excision of an islet tumour of the pancreas, but remained in a state of mental confusion with dysarthria although the blood-sugar was normal. There was no autopsy and it is possible that a cerebral vascular lesion occurred during the violent and prolonged convulsions.

Both of Anderson's cases were in diabetic boys, who may be supposed to be more liable than adults to cerebral lesions; on the other hand, children often have a very low blood-sugar without symptoms. Both boys were mentally backward before the onset of diabetes. The first, aged 13, showed a great deterioration in mental capacity after being in coma for four days. On the first day of this coma he may have been hypoglycæmic, though the evidence is inconclusive and was not confirmed by blood-sugar estimations. He was certainly not hypoglycæmic on the second and fourth days of the illness since the blood-sugar was over 180 mg. per 100 c.cm. and there were ketone bodies in the cerebrospinal fluid and glycosuria. From the second day he had fever and it seems possible that the whole of the symptoms and sequelæ were due to some such condition as encephalitis. If any hypoglycæmia preceded the mental deterioration it was of comparatively short duration. The other boy, aged 7, showed striking behaviour disorders which were at least partly due to his low mental capacity and bad environment and even his most violent actions occurred when the urine was only "more or less sugar free." In both cases the evidence that hypoglycæmia was present is not convincing; that there were other ætiological factors is certain. Moreover, when one considers the repeated and prolonged insulin coma with very low content of sugar in the blood and cerebrospinal fluid which schizophrenic patients undergo with mental improvement, it hardly seems possible that the dementia of these boys was due to hypoglycæmia.

With regard to the use of zinc protamine insulin in children, its slow action is apt to cause hypoglycæmia in the night or early morning in those who have their last meal at 5 or 6 P.M. Protamine (delay) insulin is often more suited to young children especially if given with a dose of soluble insulin.

Hove. G. M. WAUCHOPE.

1. Campbell, W. R., Graham, R. R. and Robinson, W. L. *Amer. J. med. Sci.* 1939, 198, 445.

ABACTERIAL PYURIA

SIR,—May I add to the list of causes of "sterile" pyuria mentioned in your annotation of Aug. 24 (p. 237) the abacterial pyuria due to urethritis. I had the opportunity of examining a few cases of pus from the urethra, mostly from young men, without any visible micro-organisms. These were cases of what is known as urethritis protozoica. In smears stained with Giemsa there were epithelial bodies, so called inclusions, such as are sometimes found in the conjunctival pus. The cases were subacute or chronic and resisted local treatment. They respond best to local treatment with copper sulphate (1–10% aqueous solution), and to arsenic compounds, either pentavalent (Stovarsol sodique or Spirocid) by mouth or Neosalvarsan intravenously.

Glaxo Laboratories Ltd. J. UNGAR.

INTRAMUSCULAR INJECTIONS OF VITAMINS A AND D

SIR,—Preparations of cod-liver oil have been in use for some time in the treatment of infected wounds and abscess cavities, and good results are claimed in accelerating healing and encouraging healthy granulation. It occurred to me that intramuscular injections of a fish oil rich in vitamins A and D might prove of benefit in various localised infections, and Messrs. Parke, Davis and Co. prepared me a sterilised solution of Nadola (a concentrated fish-liver oil) in olive oil which I have found valuable in staphylococcal and similar infections during the past year.

The following types of case have responded to the treatment: threatened breast abscess, perineal abscess, septic hand, infected insect bite, carbuncle, tonsillitis, threatening quinsy, developed quinsy, pre-auricular abscess, sequestrum of jaw and erysipelas of the face in an early stage. Boils and some cases of pustular eczema have also responded well.

The injections are painless, especially if the solution is warmed; occasionally there is a little local irritation around the site of injection. In feverish cases there is often a striking fall of temperature. Threatened abscesses will usually abort, but where tissue breaks down pus is localised and easily evacuated and the cavity heals rapidly. Pain is relieved early and there are prompt localisation and reduction of inflammation. In feverish cases injections are given daily for 3 or 4 days. In non-feverish cases doses on alternate days may suffice. The dose used has been 2 c.cm. made up of 0·5 c.cm. nadola in 1·5 c.cm. of olive oil. The back of the upper arm in the lower third or the buttock is a convenient site for injection, and it may be given with a large hypodermic needle.

Southampton. H. STANLEY-JONES.

SECONAL

SIR,—I was asked about eighteen months ago by Messrs. Eli Lilly to try the effects of Seconal as premedication in general surgery. I have tried it out with the help of the staff of the Wellhouse Hospital and we have found it satisfactory and reliable—by far the most reliable barbiturate of which we have had experience. The great majority of the patients come to the theatre really sound asleep. This in itself is a valuable property of the drug, but a ward sister drew our attention to the fact that it also reduced postanæsthetic vomiting. This particular sister kept records of 100 consecutive operations and found that only 8 patients vomited after operation. The ward was a women's ward, and possibly women are less likely to vomit than men. Considering all types of patients and operations on both men and women, we find that no vomiting occurs at all in 75%

of cases following seconal. When it does occur it is slight, and we never see those distressing cases of vomiting lasting sometimes two or three days after operation. We have used ether or vinesthene ether freely, so the absence of vomiting cannot be attributed to the type of anæsthetic used. We have not noticed any marked reduction in postanæsthetic vomiting after using other sedative drugs for premedication.

Wellhouse Hospital, Barnet. JOHN ELAM.

E.M.S. SALARIES

SIR,—The eighth report of the Select Committee on National Expenditure, recently published, reviews the position of the Emergency Medical Service during its first year of activity and makes recommendations and comments which, in view of the prolonged correspondence in your columns upon this subject, may interest your readers. In a letter to the *Times* of Sept. 14, 1939, I pleaded for the retention of the voluntary principle in staffing the E.M.S. in place of the scheme of practically compulsory enrolment established by the Minister before the outbreak of war. The select committee expresses its regret that this service was not recruited on a voluntary basis from the beginning. Responsibility for the scheme adopted by the Ministry of Health is squarely placed on the Central Emergency Committee of the B.M.A. and a subcommittee. The select committee comments upon the anomaly (*Lancet*, 1940, **1**, 574) by which the English members of the consultant advisory committee of the Ministry should have received remuneration not accepted by their Scottish colleagues. The select committee finds that this differentiation has no justification and recommends the withdrawal of that remuneration. It further recommends the abolition of part-time service of the consultant members of the E.M.S. by which a retaining fee of £500 a year is allowed, and suggests replacing this system by payment on a sessional basis.

The select committee was set up to constitute a check on extravagance in national expenditure and it points out that the cost per bed per annum of the salaried medical staff resulting from the measures taken for the provision of emergency service has reached in London £11, whereas the cost in England and Wales was rather more than £4 and in Scotland rather less than £1. The committee has a representative all-party constitution; its influence has already proved so great that it is probable that these recommendations will become operative at an early date.

Wimpole Street, W.1. E. GRAHAM-LITTLE.

THE NURSE ANÆSTHETIST

SIR,—Your leading article of Sept. 7 must have read as a challenge to many British anæsthetists. It will be admitted that a contingency might arise where urgent surgical work demanded attention and no medical anæsthetist was immediately available. Such an emergency, however, cannot form an honest pretext for discarding the principle in medical administration and legislation in this country that anæsthetics be given by medical men and women. For THE LANCET to suggest that in the circumstances described the choice lay between an unqualified anæsthetist and no anæsthetist at all is a quite unwarranted conclusion. Dr. Parsons's reply to the Association of Anæsthetists, far from mitigating, has aggravated the offence in the minds of British anæsthetists. Whereas one wondered whether the honorary medical and surgical staffs of Addenbrooke's Hospital had been consulted in the matter it now transpires that the honorary staff are the instigators of the policy and Dr. Parsons seeks to justify them.

It cannot surely be that the staff of the medical school of the University of Cambridge have no constructive ideas about anæsthetics. Addenbrooke's Hospital, in common with medical institutions all over the country, has been seriously depleted of its personnel in anæsthetics. Women medical resident anæsthetists are to be had and in my experience they are very efficient. They will not be called to military service and they can be retained if the authorities care to reward them in proportion to their experience and their service. Why does not the anæsthetic staff of Addenbrooke's Hospital train some of their women medical and surgical officers and promote them to be resident anæsthetists?

Anyone who has seen the nurse-anæsthetist system in the teaching hospitals of the United States of America will realise that the governing bodies of these institutions have been caught in a vicious circle. The supply of anæsthetists in America has been, and still is, very far from equal to the demand for them, so that the medical anæsthetist in the United States is very fully occupied and frankly admits that he has no time to devote to ordinary hospital cases or to the teaching of undergraduates. Nor will the amour propre of the undergraduate or the interne permit him to go to the nurse-anæsthetist for tuition or for practice in administration. Hence the continued scarcity of medical anæsthetists in the U.S.A.

He is a bold man and very short-sighted who will risk the vicious circle and support the policy that even the thin end of the wedge of the system of nurse-anæsthetist should be introduced into the teaching hospitals of this country.

Dept. of Anæsthetics, Aberdeen. J. ROSS MACKENZIE.

SIR,—What is meant by "a good anæsthetic"? Patients, surgeons and anæsthetists would all, I fancy, give a different answer to the question. Broadly speaking, the patient means a pleasant induction and no unpleasant after-effects; the surgeon means a degree of muscular relaxation sufficient for him to work unhindered; the anæsthetist means a clear airway, a satisfactory colour, pulse and respiration throughout the operation, and no crises on the table or afterwards. Doubtless the modern anæsthetic machine in skilled hands gives, as a rule, the best results. But what about the modern machine in unskilled hands? A certain surgeon whose lot it is to operate on patients anæsthetised (more or less) by young residents learning to use modern machines sighs wistfully for the good old days of the rag and bottle. He tells me that, in his hospital practice, what he calls a good anæsthetic is the exception nowadays rather than the rule. The fact is that many are called to give anæsthetics but few ought to be chosen. It seems that in this small specialty a certain temperament is necessary if success is to be achieved. But there is no reason to suppose that this temperament is found only among those holding a medical degree or diploma. Nurse-anæsthetists gave a good account of themselves in the last war. Is it to be assumed that there are no longer any nurses temperamentally suitable as anæsthetists provided, of course, that they are adequately trained?

Crediton. L. N. JACKSON.

ASCORBIC ACID AS AN INDEX OF NUTRITION

SIR,—I am not in a position to comment on Dr. Todd's suggestion that scurvy may not be due to lack of ascorbic acid; but, in his reference to the undoubted fact that fresh meat can cure scurvy, he infers that the amount of ascorbic acid present is insufficient to account for the cure. This may be so, but he may not be taking into account the quantity consumed. The Eskimo, and the white man who lives as Stefansson did, use very large amounts of fresh meat or fish, usually lightly cooked or frozen, and in such quantities sufficient vitamin may well be present.

Inverness. RUSSELL D. MARTIN, formerly M.H.O. Coppermine, N.W.T. Canada.

THE COMMON POPPY

SIR,—Among the many plants mentioned in your columns as suitable for cultivation in England for their therapeutical value I have seen no reference to the corn or field poppy (*Papaver rhœas*). This wild red poppy of the east coast, in a climate that is rarely more than moderately warm, produces a juice which when dried gives the effect of opium in similar doses. I am informed that in the southern counties the natives used to chew poppy heads for pain. From Woodville's "Medical Botany" (1793) I learn that a syrup of the flowers was then in use as an anodyne and pectoral but that "it was valued rather more for the beauty of its colour than for its virtues as a medicine." This is now used as a colouring agent only (syrupus rhœados, B.P.C.). Bruce and Dilling say of opium "there are English varieties." I have not been able to meet with any. My experiments with inspissated poppy juice have been only on myself but they suggest that the English poppy might be worth cultivating.

Saxmundham. K. HEANLEY.

Public Health

From the School Reports

THE report on the medical inspection and treatment of the children of *Kent* for 1939, written by Dr. J. W. Fox, deputy school medical officer, and presented by Dr. Constant Ponder, M.O.H. and S.M.O. of the county, has some historical importance; for during the early months of the war Kent included evacuation, reception and neutral areas so that children were shifted from one part to another of the same county. In 1940 Kent became the centre of the Battle of Britain and its child population had to be dispersed widely; the report for this year will therefore deal with what has been done with the children rather than with what has been done for them. After the war when the Kentish children return to their homes we shall be able to study what permanent influence their enforced migrations have had on them. Fortunately the health of Kentish children in the peace years has been very fully recorded. The geographical county of Kent is made up of the metropolitan area, the seaside resorts, and the land occupied by the men of Kent. The education authority is not responsible for the majority of the two former, most of the divisions of which are their own education authorities, so it happens that the county deals mainly with the truly Kentish people. At the end of the first three months of the war the normal school population of 82,949 was increased by 16,800 transferred from the evacuated areas, mainly outside the jurisdiction of the county council, but beyond closure of the schools for a fortnight there was little interference with the routine of school medicine or difficulty in extending it to the received children. Evacuation brought out in Kent, as it did in other receiving areas, that the basic school service is highly elastic, whereas the subsidiary services, chiefly nutritional aid and dentistry, have no such power of expansion. The original service was planned on a fairly generous scale for a larger child population than exists at present, whereas in few districts had dentistry developed to cover the basic needs of the resident population, and the provision of nourishment was made grudgingly as something alien to the educational system. Dr. Fox says that war-time conditions necessitate increasing the attention to nutrition and it is hoped that this may be a prelude to regular nutrition centres. Since the beginning of the century the Board of Education has recognised that children cannot benefit from education unless they are well fed and well doctored, but that the feeding and doctoring are integral parts of education is a new conception and the first definite leader for reconstruction which has emerged from the present war.

From Dr. Ian McCracken's school report for *Durham County* it is apparent that the outbreak of war caused greater dislocation of the school medical service there than it did in most parts of the country. This was to be expected, for owing to the economic state of the county in peace-time the social services have had to confront great difficulties. A table of the cases examined at the school clinics during 1939 brings out the hard case of Durham children compared with such counties as Kent which were generally prosperous. Though out of 11,385 cases treated only 65 are labelled as malnutrition, 636 were suffering from debility, 270 anæmia, 339 bronchitis, 173 rheumatic conditions, 104 chorea and 81 disorders of digestion. In districts where the level of nutrition is high the cases treated by the school department are not only few but generally capable of accurate diagnosis, whereas where nutrition is poor there are large numbers of departures from health which do not admit of definite clinical differentiation.

Small education authorities suffered in many instances by the calling up of the whole personnel. Thus Dr. G. W. Fleming reports that in *Gosport* dental treatment had to be suspended because the only school dentist had to go on service. The Board of Education should see that this does not happen and help authorities which get into unavoidable difficulties. School dentistry and medicine are the rights of every child attending a state-aided school, and the central authorities should see that he gets them.

In the first phase of the war *Scarborough* was a reception area. Dr. Fox Linton reports that in September, 1939, he had to receive 5388 evacuees which subjected the school medical service to great strain. This is understandable, for the average attendance at the elementary schools in peace-time is only about 4000. The children came from Hull, Middlesbrough and West Hartlepool and naturally were not up to the standard of cleanliness to which Scarborough is accustomed. For the first fortnight the school clinic was turned into a cleansing station and an emergency cleansing station was opened on Sept. 3. Many children required re-clothing. Scarborough, being a holiday resort, should have plenty of room for the reception of large numbers of refugees, but the billeting of verminous or objectionable persons is a matter of great difficulty, the full extent of which was not recognised before evacuation took place. Scarborough has a special class for the treatment of speech defects. In 1939 the number of children admitted to the class was 57, of which 48 were boys. Half of them were cured. Lispers and lallers can usually be cured fairly easily but stammerers require long treatment which must be started early to be successful.

Obituary

PETER BERNARD SPILSBURY

B.M. OXFD.

Gillman, Oxford.

On Sept. 16 Peter Spilsbury was killed by enemy action while on duty at St. Thomas's Hospital. He was the second son of Sir Bernard Spilsbury and was 25 years of age. Educated at Rugby and Magdalen College, Oxford, he obtained a second class in the final honours school of physiology in 1937. He entered St. Thomas's Hospital medical school and took his B.M. last July. He had just begun his duties as house-surgeon to Mr. W. H. C. Romanis but had not then decided whether he was going to be physician or surgeon.

INFECTIOUS DISEASE IN ENGLAND AND WALES

DURING THE WEEK ENDED SEPT. 7, 1940

Notifications.—The following cases of infectious disease were notified during the week: smallpox, 0; scarlet fever, 1449; whooping-cough, 1055; diphtheria, 929; enteric fever, 126; measles (excluding rubella), 5949; pneumonia (primary or influenzal), 371; puerperal pyrexia, 150; cerebrospinal fever, 107; poliomyelitis, 42; polio-encephalitis, 4; encephalitis lethargica, 2; dysentery, 57; ophthalmia neonatorum, 93. No case of cholera, plague or typhus fever was notified during the week.

The number of civilian and service sick in the Infectious Hospitals of the London County Council on Sept. 6 was 959, made up of: scarlet fever, 174; diphtheria, 191; measles, 201; whooping-cough, 27; enteritis, 25; chicken-pox, 31; erysipelas, 24; mumps, 6; poliomyelitis, 1; dysentery, 8; cerebrospinal fever, 30; puerperal sepsis, 26; enteric fevers, 40; german measles, 2; other diseases (non-infectious), 88; not yet diagnosed, 85.

Deaths.—In 126 great towns, including London, there was no death from smallpox, 1 (0) from scarlet fever, 1 (0) from enteric fever, 2 (0) from whooping-cough, 8 (0) from measles, 36 (0) from diphtheria, 46 (7) from diarrhœa and enteritis under 2 years, and 11 (0) from influenza. The figures in parentheses are those for London itself.

The fatal case of enteric fever was at Rotherham. Liverpool reported 6 deaths from diphtheria, Nottingham and Plymouth each 3.

The number of stillbirths notified during the week was 207 (corresponding to a rate of 38 per thousand total births), including 20 in London.

Notes, Comments and Abstracts

MODIFIED BRAUN'S SPLINT

By F. P. Fitzgerald, M.B. Dubl., F.R.C.S.I.

FRACTURE AND ORTHOPÆDIC REGISTRAR AT THE ROYAL NORTHERN HOSPITAL, LONDON ORTHOPÆDIC SURGEON TO THE WELLHOUSE HOSPITAL, BARNET (E.M.S.)

Braun's splint for fractured femur has been altered in almost every way since Böhler reintroduced it with his own modification. Many of the alterations are cumbersome and costly. Those described here are simple and inexpensive.

FRACTURES JUST BELOW THE LESSER TROCHANTER

The upper fragment is strongly flexed. The ordinary Braun's splint is not satisfactory even when the patient is propped up on a high bed rest. By hinging the splint so that the angles can be varied it is possible to make the oblique bars vertical (fig. 1). Then, with the usual skeletal traction through the crest of the tibia and with a pulley from the overhead beam of a Morrison's frame (or any balkan beam), the lower fragment may be brought into line with the upper.

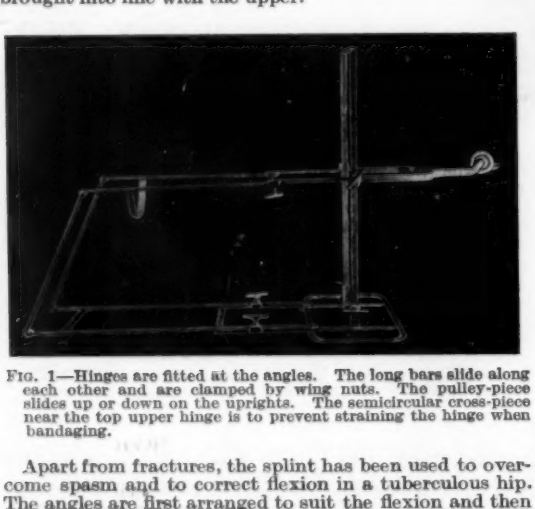


Fig. 1—Hinges are fitted at the angles. The long bars slide along each other and are clamped by wing nuts. The pulley-piece slides up or down on the uprights. The semicircular cross-piece near the top upper hinge is to prevent straining the hinge when bandaging.

Apart from fractures, the splint has been used to overcome spasm and to correct flexion in a tuberculous hip. The angles are first arranged to suit the flexion and then gradually altered until the required inclination is achieved (fig. 2). The splint can be taken to pieces and packed into a small space (fig. 3).

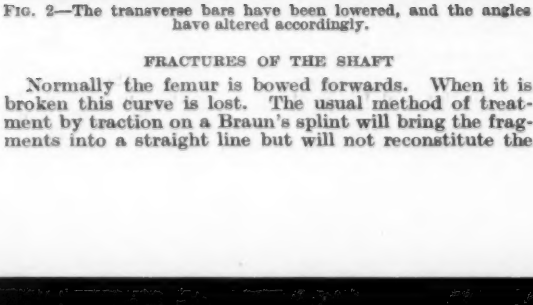


Fig. 2—The transverse bars have been lowered, and the angles have altered accordingly.

FRACTURES OF THE SHAFT

Normally the femur is bowed forwards. When it is broken this curve is lost. The usual method of treatment by traction on a Braun's splint will bring the fragments into a straight line but will not reconstitute the arc. This difficulty has been overcome by fitting two bowed pieces of metal to the oblique bars of the splint (fig. 4). The bandage used to pad the splint is wound tightly round them and then round the upper horizontal bars.

Fig. 3—Assembled for storage or transport.

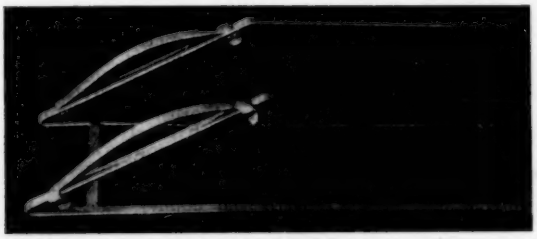


Fig. 4—The bows in place.

These expedients have not been tried out exhaustively, but the results in the few cases treated have been encouraging. Both appliances were made for me by the Medical Supply Association. The cost of the splint is 35*s*. The bows cost 9*s*. a pair.

TESTS OF CIRCULATORY EFFICIENCY

In these days of scientific medicine, when clinical impressions are being gradually ousted by objective measurements and the functional efficiency of any organ must be gauged by some precise yardstick, the cardiovascular system should be capable of accurate assessment. Of the many tests recommended—exercise tolerance, venous pressure, circulation time, cardiac output, vital capacity—not one, used singly, yields any more information than a careful examination of the patient and a full and accurate case-history. Measurements of circulation time and cardiac output are too complicated for routine clinical use, and the exercise-tolerance test seldom gives additional information of value. The response to undressing, for instance, usually provides as much, if not more, information about the functional capacity of the heart than climbing steps or touching toes; and neither of these procedures is as accurate a guide as the patient's statement that he can manage on the level so long as he does not hurry, but the moment he tries to hurry or starts to climb stairs he becomes short of breath or develops pain in the chest. Again, attempts to simplify laboratory procedures so that they can be carried out by the clinician without any apparatus or technical knowledge are seldom helpful. The most successful of these—the use of the veins in the neck as a guide to the venous pressure—cannot be given the significance which some ascribe to it. As one of several pieces of information it is of value, but by itself it gives little help. These various procedures may add to our knowledge and throw light on the mechanism of the cardiovascular system in health and disease; but we must realise that the cardiovascular system is a complicated piece of mechanism whose functions are closely interwoven with the other systems of the body. In other words, the simpler the test the less likely is it to provide reliable information. There is a point beyond which the process of simplification cannot be carried, and we must try to obtain as much help as possible from the patient's history and reactions to ordinary clinical methods. This is a safeguard against applying the results of the laboratory to clinical practice in an entirely uncritical spirit.

QUARTERLY JOURNAL OF MEDICINE

THE July issue contains the following papers, together with a report of the proceedings of the thirty-fourth annual general meeting of the Association of Physicians:

POISONING BY METHYL MERCURY COMPOUNDS. By Donald Hunter, Richard R. Bomford, and Dorothy S. Russell (London Hospital). The authors report four cases of poisoning, resulting from the inhalation of methyl mercury iodide or nitrate by workmen engaged in manufacturing the latter compound as a fungicidal dressing for seed (wheat and barley). The poison affected the nervous system only, producing severe ataxia, dysarthria, and constriction of visual fields, with sometimes extensor plantar responses. There was little sign of recovery in one to three years, though re-education could reduce the disability. In animal experiments methyl mercury compounds selectively damaged peripheral nerves, posterior spinal roots, the posterior columns, and the granular layer of the middle lobe of the cerebellum.

LIVER FUNCTION IN THYROTOXICOSIS. By N. F. Maclagan and F. F. Rundle (Westminster Hospital). Blood galactose estimations, made at half-hour intervals for two hours after administration of 40 grammes of galactose by mouth, yielded evidence of diminished galactose tolerance—i.e., impaired liver function—in at least 30 out of 41 thyrotoxic patients. The results of the test can be roughly correlated with B.M.R. and the clinical severity of the disease. Galactose tolerance improves slightly with iodine treatment, but greatly (though not always to normal) after partial thyroidectomy. In rabbit experiments thyroxin injection impaired the animals' tolerance to intravenously injected galactose, and the livers showed focal necroses. The test in man promises to be of value in the management of patients.

THE ACTION OF PARASYMPATHETIC-MIMETIC DRUGS IN ASTHMA. By H. H. Moll (Leeds). Acetyl-β-methylcholine injected subcutaneously in 10 mg. doses, induced asthma-like attacks in nearly all of 28 asthmatic subjects, irrespective of the dependence of their asthma on infective, allergic, psychological or other factors. Atropine and adrenalin cut short the induced attacks equally well, and 500 mg. ascorbic acid given intravenously abolished them a little more slowly. Control subjects showed general signs of parasympathetic stimulation but developed no chest symptoms. The author argues that the asthmatic's abnormal sensitivity lies in his bronchial system rather than in his vagal centre, and that lung damage is an essential factor in determining it.

A SUSPECTED CASE OF LEPROSY

IN the 15th century records of the King's closed correspondence (as distinct from letters which were sent open) were kept in what are called close rolls. Mr. Kenneth Ledward, an assistant keeper of the Public Record Office, has sent us from the roll of the eighth year of the reign of King Edward IV an extract from a commission of doctors called upon to testify on a suspected case of leprosy. Joan de Nightyngale of Brentwood in Essex was thought by her neighbours to be a leper, and on July 10, 1468, the King issued a writ directing the sheriff of Essex "to take with him discreet men of the county who have the best knowledge of that disease and of her person to repair to her and cause her to be examined in their presence, and if he shall find her a leper to remove her to a solitary place, there to dwell as the manner is, as the King has learned that she is leprous, and has her conversation among men of that county in public and private places, refusing to move to a solitary place, and his will is to guard against such peril, and do what is lawful and accustomed." Joan seems however to have got wind of the writ and before it could be executed "came into chancery for remedy and relief." The chancellor decreed that William Hatteclyff, Roger Marchall and Dominicus de Serego should be consulted to "certify in chancery what they should perceive by the science of medicine." Hatteclyff, who was a man of some standing at that time, combined the offices of physician and secretary to the king. The doctors' report to the King on Joan was as follows:

"First they did consider her person, treating and handling her; and making their discourse of all the symptoms of the disease whether it were found in her or no, and after view and consideration of all things needful for true knowledge of what was in doubt, they found that she was not leprous, and needed not to be kept apart: that they are taught by medical science that the symptoms of leprosy are many: that there are four forms, namely alopecia, tiria (satyriasis), leonisia and elefancia, and each may be distinguished by the symptoms: that in this case by discourse of five and twenty best known symptoms and more, they found the woman could not be proved leprous, thereby, or by a sufficient number of them; and that this was sufficient to free her, for none could suffer from the disease without great part thereof being found: and that passing in review forty and more distinguishing symptoms, they found her not marked by either of the four forms aforesaid."

We are not told whether such profound wisdom enabled Joan to keep her freedom.

LEBANON HOSPITAL FOR MENTAL DISEASES

THE annual report of the mental hospital at Asfuriyeh, near Beirut, reaches us at a moment when events in Syria are nearing a crisis. The effects of the war were quickly felt. The influx of private patients from Egypt, Palestine and other neighbouring lands ceased and their place was taken by military and Government cases. Even with the new house for 60 chronic male cases opened last September, increasing the total beds to 500, some cases had to be transferred in order to free 150 beds for possible civilian casualties by arrangement with the French Red Cross Society. In the last war this international hospital, then consisting of 100 beds, stood in Islam, and its medical director, the late Dr. Henry Watson Smith, was virtually a prisoner. But while war and famine prevailed outside, the Turks respected the hospital as *Wakf*. Later it gave invaluable service to General Allenby's troops during an influenza epidemic. Now with its 500 beds the hospital may be called on for yet larger service. Dr. Stewart Miller, the present medical director, has been head of the mental hospital at Khanka, near Cairo, with its 1700 beds, the matron has had 25 years' experience and all the sisters have had general as well as mental training. The London office of the hospital is at Drayton House, Gordon Street, W.C.1.

From a considerable experience of various forms of shock therapy during the last year Dr. Miller has reached the following tentative conclusions. In schizophrenic reaction states that are in any way chronic none of them procures complete recovery or lasting mental benefit. Insulin therapy benefits the patient physically. In acute schizophrenic states non-specific fever therapy yields results as satisfactory as any other, and at less risk and expense. In manic-depressive states non-specific fever therapy will effectively shorten the duration of the attack with less risk to the patient and at less cost than with other forms of treatment.

DOMICILIARY MIDWIFERY SERVICE IN LONDON

AT present the London County Council is paying voluntary hospitals £2 6*s*. 10*d*. for each confinement attended by a midwife acting alone or when a medical student is present, and £1 17*s*. 6*d*. for each confinement attended by a midwife accompanied by a pupil midwife. District nursing associations receive £2 14*s*. for each confinement attended by a midwife. At its last meeting the L.C.C. increased the first and third of these payments to £3 5*s*. and £3 12*s*. 6*d*. respectively; the payment for a midwife accompanied by a pupil is also to be £3 5*s*. unless the Ministry of Health renews its grants for the training of pupil midwives. Sterile midwifery outfits costing 7*s*. 3*d*. are provided free of charge to nursing associations; voluntary hospitals provide their own. Midwives employed by council or voluntary organisation are to receive £2 10*s*. instead of £2 for a first confinement, £2 instead of £1 10*s*. for subsequent confinements or maternity nursing.

GLAXO LABORATORIES Ltd. inform us that the growing demand for Adexolin (concentrate of vitamins A and D) and Fersolate (ferrous sulphate G.L.) has made it possible to reduce the prices of these preparations.

CORRIGENDA.—The director of medical services in Southern Rhodesia, mentioned on p. 402 of our last issue, is Dr. Andrew Paton Martin.

The reference to Miller and Simpson in the paper by Dr. Bentley and Dr. Smithwick in our issue of Sept. 28 (p. 391) should read: Miller, F. R. and Simpson, H. M. (1924) *Trans. roy. Soc. Can.* Ser. III, **18**, *Sect.* V, 147.

GET YOUR STAMPS FROM BART'S

THE war interrupted the Lord Mayor's appeal for the Bart's rebuilding fund but the need remains, and the appeals department of the hospital go quietly on with a job which will still be important when the immediate expenses of the nation are a memory. They are anxious to sell large numbers of stamps which, unlike the post-office variety, have gone down in price. As the editor of the *St. Bartholomew's Hospital Journal* points out, they are nice and sticky and can be used to seal up envelopes which have been once or twice through the post—a pleasant paper-saving sport. The designs on most of the stamps are commendably austere. If they are quickly sold is it possible that the hospital might consider a fresh edition, derived from the pages of "Candid Camera"? But we must buy up these first; a sheet of twelve costs 2*d.*, and can be obtained from the Appeals Department of the hospital.

BY WOMEN FOR WOMEN

THOUGH the "purdah" habit is breaking down in many districts in India, yet women patients are seeking treatment in increasing numbers at Dufferin hospitals which are staffed by women, and the twenty-sixth report of the Women's Medical Service for India,[1] which developed from the Countess of Dufferin's Fund to meet the medical needs of Indian women observing seclusion, reports that the medical cadre of 47 officers maintained their reputation for efficiency during 1939 in spite of many difficulties. At The Lady Hardinge Medical College and Hospital in Delhi 137 women students are being trained, and the reports of the different professors indicate the variety of clinical material available for teaching. The many-sided activities of these students now include hockey, tennis and swimming. Some of the provincial Dufferin hospitals are said to be short of money, because many patients able to contribute towards the cost of their treatment continue to make use of facilities which should be reserved for the poor. The need for encouraging Indian girls of good family to train as hospital nurses is emphasised, but the living conditions provided for them by local hospital committees must be improved. An interesting innovation during the year was a short course for junior service officers in hospital administration.

Medical News

Hospitals Day, Oct. 8, 1940

Next Tuesday the hospitals of London are holding their combined street collection. Last year the amount collected was double that collected in any previous year, and three quarters of the October collection was transferred to the Red Cross. This year when needs are so great it is hard to imagine any need greater than that of the hospitals in London, which, as Mr. MacDonald put it on Tuesday, are coolly carrying on in the front line.

National Institute for the Blind

Lord Nuffield's gift of £10,000 has made it possible for the institute, in conjunction with local societies for the blind and the responsible local authorities, to assist blind civilians. Particulars of any men, women or children whose sight has been injured during air-raids should be sent to the chairman of the institute at 224, Great Portland Street, London, W.1.

M.O.H. for Swindon

Dr. Dunstan Brewer who has held this post for 20 years retired at the end of last month, and on the 16th his colleagues met to do him honour and give him a silver rose bowl. In making the presentation Dr. R. P. Beatty, senior practitioner of the district, said he hoped Dr. Brewer would enjoy many years of active retirement, for he was not the type of man to sit still and do nothing. The local education committee also met to record their appreciation of Dr. Brewer's services to the children of the borough.

The Charterhouse Rheumatism Clinic is continuing treatment of patients including the X-ray department and laboratories.

1. Fifty-fifth annual report of the National Association for supplying medical aid by women to the women of India (Countess of Dufferin's Fund, including the Women's Medical Service), for the year 1939. Simla: Government of India Press.

Honours in the Services

The O.B.E. has been awarded to Major Ralph Brooke, F.R.C.S., R.A.M.C., T.A., for gallant and distinguished services in action in connexion with operations in Norway. The military cross has been awarded to Lieut. A. E. Cooper, M.R.C.S., R.A.M.C., and Lieut. H. A. Dougan, M.B. Dubl., R.A.M.C., for gallant and distinguished services in the field.

Casualties

The following casualties are announced:—

Missing, presumed killed.—Temp. Surgeon Lieutenant H. A. Wallace, M.B. Camb., R.N.V.R., and Prof. Temp. Surgeon Lieutenant E. I. Smith, M.B. Glasg., R.N.V.R.

Wounded.—W.S. Captain F. Murray, R.A.M.C.

Chadwick Lectures

It has been decided to postpone these lectures which were to have been delivered this autumn. Due notice will be given when they are to be resumed.

Royal Society of Medicine

On Tuesday, Oct. 8, at 4.30 P.M., Group Captain C. P. Symonds will deliver his presidential address to the section of psychiatry of this society. He will speak on the neurological approach to mental disorder.

Biochemical Society

A meeting of this society will be held at the department of biochemistry of the University of Oxford today (Saturday) at 2·15 P.M.

The outpatient department of St. John's Hospital for Diseases of the Skin at 5, Lisle Street, Leicester Square, London, W.C.2, announces certain changes in arrangements. Clinics are being held daily from Monday to Friday, from 1 to 3 P.M. The evening clinics and inpatient departments are closed until further notice.

Arrangements have been made with St. Bartholomew's Hospital for the reception of "emergencies" who should not now be sent to the City of London Maternity Hospital.

Appointments

BURNET, W. S., M.D. Glasg., D.P.H.: chief asst. M.O.H for Stirling.
BUTLER, DORA M., M.B. Lond., D.P.H.: temp. asst. M.O. (maternity and child welfare) for Northampton.
COLLINS, ANNIE, M.B. Belf.: temp. asst. M.O. for Heston and Isleworth.
FRANKLIN, J. L., M.D. Camb., M.R.C.P.: physician for diseases of the skin to the Westminster Hospital.
RAFTERY, LILIAN, M.R.C.S.: surgical registrar at the Elizabeth Garrett Anderson Hospital, London.

Births, Marriages and Deaths

BIRTHS

EVERETT.—On Sept. 28, at Sutton, the wife of Mr. A. D. Everett, F.R.C.S., of Leatherhead—a daughter.
FENTON.—On Sept. 19, at Datchet, the wife of Major C. E. Fenton, R.A.M.C., of Barking, Essex—a son.
MEREWETHER.—On Sept. 26, in London, the wife of Major Henry Osborne MacCabe Merewether, R.A.M.C., of Folkestone—a daughter.
PUGH.—On Sept. 17, in Oxford, the wife of Lieutenant Griffith Pugh, R.A.M.C.—a son.
STANLEY.—On Sept. 24, at East Grinstead, the wife of Dr. Roger Stanley—a son.
WHITELAW.—On Sept. 19, at Hertford, the wife of Dr. Alan Whitelaw—a daughter.
WHITTERIDGE.—On Sept. 24, in Oxford, the wife of Dr. David Whitteridge—a daughter.

MARRIAGES

HILEY—SHORT.—On Aug. 23, at Halifax, Nova Scotia, Charles Arthur St. Clair Hiley, Surgeon Lieutenant, R.N.V.R., to Ena Short.
WARBURTON—LEE.—On Sept. 24, at Newtonmore, Inverness-shire, John Rollo Noel Warburton, Lieut.-Colonel, R.A.M.C., to Mary Hartwell Lee.
WITT—ALLOTT.—On Sept. 28, at Harrogate, Robert Witt, M.R.C.S., to Margaret Allott.

DEATHS

HOYLAND.—On Sept. 26, at Ipswich, Stanley Stenton Hoyland V.D., M.D. Durh., late Colonel A.M.S., T.R., aged 84.
SPILSBURY.—On Sept. 16, at St. Thomas's Hospital, Peter Bernard Spilsbury, B.M. Oxfd, aged 25.
THOMSON.—On Sept. 25, Frederick George Thomson, M.A. Camb., M.D. Lond., F.R.C.P., of Bath.
ZEAL.—On Sept. 17, as a result of enemy action at sea, Betty Margaret Zeal, M.B. Lond., D.P.M., aged 30.